Interdisciplinary Management of Malignant Ovarian Tumors in the Pediatric and Adolescent Age Group

Anam Khaja, MD[1,*], Lindsay Frazier, MD[2], Brent R. Weil, MD, MPH[3], Christopher B. Weldon, MD, PhD[4], Marc R. Laufer, MD[1,5], Jessica Shim, MD[1,6]

[1] *Division of Gynecology, Boston Children's Hospital, Boston, Massachusetts*
[2] *Dana Farber/Boston Children's Cancer and Blood Disorders Center, Pediatrics, Harvard Medical School, Boston, Massachusetts*
[3] *Department of Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts*
[4] *Department of Anesthesiology, Critical Care, and Pain Medicine, Department of Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts*
[5] *Department of Surgery, Boston Children's Hospital, Center for Infertility and Reproductive Surgery, Brigham and Women's Hospital, Obstetrics, Gynecology, and Reproductive Biology, Harvard Medical School. Boston, Massachusetts*
[6] *Division of Gynecology, Department of Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts*

A B S T R A C T

Malignant ovarian neoplasms are uncommon in the pediatric and adolescent population. Imaging and tumor markers help to guide the preoperative risk/benefit analysis for planned surgical management, which is the mainstay of therapy. An interdisciplinary approach should be taken in the management of this vulnerable population from diagnosis through post-treatment surveillance. In this review, the initial evaluation, risk stratification, and management of various types of malignant ovarian masses will be addressed, with a special focus on how to optimize an interdisciplinary approach to ovarian masses.

Introduction

Ovarian masses are rare in the pediatric and adolescent population, with most being benign ovarian neoplasms or physiologic ovarian cysts. However, up to 20% might be malignant, with most being of germ cell origin, which is in contrast to adults, in which most ovarian malignancies are of epithelial origin.[1–3] Surgery is the mainstay of treatment in the non-adult population, regardless of histopathological subtype. However, special consideration secondary to the young age of this cohort must be given to aspects of their care (eg, fertility preservation) when feasible. Therefore, the medical, surgical, and reproductive health outcomes in young patients with ovarian malignancies are best addressed by an interdisciplinary approach.[4,6–10] This article will review the initial evaluation, risk stratification, and management of the various types of malignant ovarian neoplasms in the pediatric and adolescent population, with a focus on interdisciplinary collaboration and management.

Evaluation

Ovarian masses can present clinically in a variety of ways. Most commonly, patients will have abdominal pain (but infrequently from ovarian torsion), but they can also present with abdominal swelling, a palpable mass, menstrual irregularities, gastrointestinal symptoms (vomiting), virilization, precocious puberty, or asymptomatic. Oftentimes due to the varied clinical presentation of a malignant ovarian neoplasm, the first clinician to evaluate an affected patient is a pediatrician or an emergency department provider.[4,7–10] Depending on the setting and resources available, referrals or consults can then be made to a variety of specialties depending on institutional preference and/or practice patterns, including gynecology, pediatric surgery, oncology, or endocrinology.

Evaluation of ovarian masses begins with a thorough medical history and physical exam. In premenarcheal children, it is imperative that a thorough history of pubertal development be obtained as precocious puberty can be a presenting sign of an ovarian mass. This is also important in the adolescent patient, in addition to obtaining a menstrual history, as menstrual irregularities and virilization can be indicative of a neoplasm. For all patients, family history is critical as this is where genetic syndromes can often be first recognized. Although most ovarian cancers are due to somatic mutations, there are inherited predisposition syndromes that typically follow an autosomal dominant pattern. In an asymptomatic child or adolescent, it is not recommended to screen for ovarian cancer; however, care must be taken if a genetic syndrome is identified or suspected based on family history. If such a genetic syndrome is a consideration based on history and also consistent with the patient's clinical picture, genetic counseling becomes crucial, with all subsequent discussions acknowledging and addressing reproductive implications of the proposed care to be provided.[11–13]

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* *Address correspondence to*: Anam Khaja, 333 Longwood Ave Boston, MA 02215, Tel:. 617-355-7648.

E-mail address: akhaja4290@gmail.com (Anam Khaja).

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A thorough physical exam can assess for a pelvic mass, in addition to other symptoms such as precocious puberty and virilization. An abdominal exam can determine if a mass or fullness is present, including even more serious sequelae such as ascites. A vaginal examination involving a speculum or bimanual palpation is typically not indicated in the pediatric or non-sexually active adolescent populations as it could be traumatic with little utility. Alternatively, a rectal exam might be helpful in assessing the size of the mass. Features worrisome for malignancy include a large fixed mass.

Once there is suspicion for an ovarian mass, imaging should be obtained. Two views of the abdomen (upright, supine) by plain radiographs should be the first step to evaluate for non-gynecological processes or problems to ensure the correct diagnostic algorithm is being utilized. Furthermore, sometimes calcifications located within tumors can be identified to aid in the differential for both ovarian and non-ovarian neoplasms. The first dedicated imaging modality of choice for a concerning pelvic mass is a transabdominal ultrasound of the pelvis.[14,15] Transvaginal ultrasound is unnecessary and should not be performed in pediatric patients, particularly if they have not been sexually active. Ultrasound can be helpful in differentiating benign and malignant ovarian lesions. Masses can appear cystic, solid, or heterogenous and should be described as such, in addition to documenting the size of the mass. Internal hemorrhage, fibrosis, and necrosis can all result in a heterogeneous appearance of the mass on ultrasound.[14] A thorough history can be helpful in interpreting the imaging results, such as using the patient's last menstrual period to estimate when ovulation has occurred.

If ultrasound imaging is indeterminate or concerning for possible malignancy, blood tests and further imaging are warranted. A pregnancy test and serologic tumor marker assessments should be obtained, as specific substances could be elevated in the setting of its associated neoplasm (Table 1).[1] Generally, abdominal and pelvic magnetic resonance imaging (MRI) is recommended in pediatric patients to spare the effects of ionizing radiation when possible. An MRI could require additional steps such as administering anesthesia, but it is the best exam for identifying occult pathology in the contralateral ovary, associated lymph node involvement in the pelvis or abdomen, evidence of liver lesions, peritoneal surface involvement, or other non-ovarian tumors. Additional imaging might be considered (computed tomography of the chest, positron emission tomogram scan) to assess for metastatic disease, too, when warranted.

Further imaging and blood work might not be appropriate if the patient is being evaluated in the emergency department, however. Patients with evidence of an acute abdomen should be urgently evaluated to assess for time-sensitive diagnoses (ovarian torsion, appendicitis, bowel obstruction, etc.) that might trump a formal neoplastic evaluation at presentation. A common occurrence is a patient who presents with ovarian torsion and an ovarian mass, which on ultrasound has the classic appearance of a complex-appearing adnexal mass due to internal hemorrhage, necrotic tissue, and tissue edema. Surgery should not be delayed to perform a complete diagnostic and staging evaluation if the patient requires urgent/emergent surgical intervention for any diagnosis (including ovarian torsion). Reassuringly, the rate of malignancy in torsed ovaries is less than 2%.[16] However, because the rate is not zero, the patient and family should be counseled on the need for potential future surgeries. In our practice, we often perform staged procedures for torsion, meaning that the initial emergent surgery involves detorsion of the adnexa. At the time of this first operation, tumor markers can be obtained as indicated. The cystectomy or removal of the mass in not immediately performed due to edema and loss of normal anatomy. We have found that by 2 weeks postoperatively, normal anatomy is restored and edema has resolved. By this time, if malignancy is suspected, tumor markers will have resulted and the appropriate risk assessment will have taken place to determine if the second procedure will involve simple cystectomy or oophorectomy with staging.

Table 1
Tumor Markers[1]

Serum tumor marker	Associated neoplasm
CA-125	Epithelial tumors
	Immature teratoma
Alpha-Fetoprotein (AFP)	Endodermal sinus tumors
	Embryonal carcinoma
	Mixed germ cell tumors
	Immature teratoma
	Polyembryoma
Human chorionic gonadotropin (hCG)	Choriocarcinoma
	Embryonal carcinoma
	Mixed germ cell tumors
	Polyembryoma
	Dysgerminoma
Carcinoembryonic antigen (CEA)	Serous tumors
	Mucinous tumors
Lactate dehydrogenase (LDH)	Dysgerminoma
	Mixed germ cell tumors
	Endodermal sinus tumors
	Embryonal carcinoma
	Immature teratoma
Estradiol	Thecoma
	Adult granulosa cell tumors
	Dysgerminoma
	Immature teratoma
Testosterone	Sertoli cell tumors
	Leydig cell tumors
Inhibin	Granulosa cell tumors
	Sertoli-Leydig cell tumors
Anti-Müllerian hormone (AMH)	Granulosa-theca cell tumor

Risk Assessment

Unless malignancy is suspected based on imaging characteristics and tumor marker levels, most benign ovarian masses are simple-appearing cysts that can be managed expectantly as functional ovarian cysts will involute and resolve spontaneously. Persistent cysts/masses are typically nonfunctional and are usually not malignant and can be managed conservatively via excision of the lesion with ovary-preserving surgery. Unfortunately, numerous studies have shown that the rate of oophorectomy among benign masses remains high in the pediatric and adolescent population.[2,5] The rate of oophorectomy has also been indepen-

dently associated with provider specialty, with adult gynecologists and pediatric surgeons performing oophorectomy at higher rates than pediatric gynecologists.[2] Thus, it is critical that a standardized approach be developed in stratifying ovarian masses to decrease the rate of unnecessary oophorectomy. The combination of imaging, tumor marker results, and clinical picture can help to risk stratify an adnexal mass as benign or malignant. This is incredibly important to optimize the use of ovary-sparing surgery as opposed to immediate oophorectomy, which can have significant consequences for future fertility.[5]

In the adult population, there are validated models that can aid in risk stratification. The International Ovarian Tumor Analysis Group (IOTA) has developed a risk stratification model known at the Simple Rules, which are based on ultrasound findings.[17–19] B-features are those characteristic of benign lesions and include the presence of a unilocular cyst, less than 7-mm solid component if present, acoustic shadows, smooth multilocular tumor with the largest diameter of less than 100 mm, and no doppler blood flow within the mass. M-features are those characteristic of malignant lesions and include an irregular solid tumor, ascites, at least 4 papillary structures, an irregular multiloculated solid tumor with a diameter of greater than 100 mm, and very strong doppler blood flow within the mass. Benign lesions only have B-features, and malignant masses only have M-features. If there are conflicting features or no features, the results are inconclusive. When the Simple Rules were validated by the IOTA group, as well as other research teams, the malignancy rate in cases classified as benign ranged from 1% to 9%, in cases classified as malignant ranged from 69% to 94%, and in inconclusive cases ranged from 13% to 53%. Other models used in the adult population include the Risk of Malignancy Index (RMI), the Risk of Ovarian Malignancy Algorithm (ROMA), OVA-1, and the IOTA regression models.[17,18] More recently, the American College of Radiology sponsored an international multidisciplinary committee that created the Ovarian-Adnexal Reporting and Data System (O-RADS) ultrasound risk stratification and management system, which assigns an ovarian mass a risk category based on imaging characteristics.[20] This system was developed for average risk patients without acute symptoms and based off of findings of transvaginal ultrasound imaging.[20] Although not perfectly applicable for the pediatric and adolescent population, the O-RADS system could be helpful in guiding optimal imaging follow-up and when referrals should be made.

In contrast to the adult population, in the pediatric and adolescent population, there are no validated risk stratification models for ovarian masses, but studies have developed several promising strategies to do so.[5, 21–23] Depoers et al[5] published a simple preoperative scoring system for adnexal masses with normal tumor markers on the basis of tumor size and cystic content. Pending these ultrasound findings, a numerical score was used to classify the mass as low risk, middle risk, or high risk for malignancy. Low-risk masses underwent ovarian-sparing surgery, and high-risk masses underwent oophorectomy. The middle-risk masses had to undergo further evaluation and discussion before management was decided. This middle risk category is one where a multidisciplinary discussion can help optimize fertility sparing surgeries. Depoers et al[5] suggested that masses classified as middle risk should all be evaluated at minimum with an MRI. A previous study by Madenci et al[23] described a risk stratification system on the basis of tumor markers and imaging characteristics. Comparing the systems developed by Depoers et al and Madenci et al, the former led to ovarian-sparing surgery in 57% of masses vs 54.5%.[8] Ye et al[24] suggested that all tumors greater than or equal to 10 cm with solid/complex components on imaging and abnormal tumor markers warrant oophorectomy.

At our institution, there are weekly multidisciplinary tumor boards where patients are discussed to optimize management. In these meetings, there is joint discussion on how to best risk stratify a patient, including what the best surgical approach should be. At each meeting, medical oncology, pediatric surgery, and radiology are present. If there is an adnexal mass, gynecology will also join the meeting. Although no formal risk assessment algorithm is utilized in these meetings, each patient with an ovarian mass is presented by the gynecology team. The medical oncology service will then interpret the tumor marker results, and the radiology team will review any imaging characteristics that are suspicious for malignancy. After discussion of the tumor marker results and imaging, gynecology and pediatric surgery will review the optimal surgical approach. At our institution, gynecology is typically the primary surgeon and will enter the abdomen, perform the oophorectomy, and close. However, pediatric surgery will also be involved in all cases, as they will perform intraoperative lymph node assessment and lymphadenectomy if appropriate. Additionally, they will further assist if there are extensive adhesions or involvement of the bowel.

Management

Malignant ovarian neoplasms are initially managed surgically. As discussed above, imaging and tumor markers help to guide preoperative planning. However, prior to surgery being performed, oncology service should be involved. Hence, we would advocate for a multidisciplinary evaluation involving the surgical teams (gynecology and pediatric surgery where applicable), oncology, and radiology to review the case details and optimize management to provide realistic expectations for the patient and her family. Depending on the institution, adult gynecologic oncologists may be involved in the medical and/or surgical management of the patient as well. It is imperative that an initial discussion on fertility also be addressed at this time, especially in the case of bilateral tumors. Some institutions might have access to an oncofertility program, which should also be enlisted to aid patients and families to pursue options to preserve their fertility at the initial or subsequent interventions. This latter scenario is especially true in situations where an ovary is removed in the conduct of the operation, and then postoperative adjuvant (gonadotoxic) chemotherapy is utilized for cure.

When malignancy is suspected, the surgical approach is typically via laparotomy to ensure that adequate staging is completed.[1] Surgical staging is crucial because it helps to

Table 2
Management Overview of Malignant Ovarian Neoplasms[25]

Type of tumor	Subtypes	Surgical management	Medical management	Postoperative surveillance
Germ Cell	Dysgerminoma Immature teratoma Yolk sac tumor Embryonal carcinoma Polyembryoma choriocarcinoma	Peritoneal cytology, resection of tumor, biopsy or excision of suspicious implants or lymph nodes	Adjuvant chemotherapy with bleomycin, etoposide, and cisplatin for advanced stage disease **not shown to be helpful after complete resection of immature teratomas	No established strategy. Can consider obtaining tumor markers monthly, imaging every 2–4 months, and office visits every 2–4 months for the first 2 years
Sex cord Stromal	Granulosa cell Sertoli Leydig cell gynandroblastoma	Unilateral salpingoophorectomy with staging	Platin based chemotherapy for advanced stages	No established strategy. Can consider monitoring tumor markers that were elevated every 2–4 months, and office visits every 2–4 months for the first 2 years followed by every 6 months thereafter.
Epithelial cell	Borderline	Unilateral salpingoophorectomy		Office visits every 3–6 months for the first 5 years followed by annually for the subsequent 10–20 years with physical exam, imaging, and tumor markers if initially elevated
	Malignant epithelial	Should be managed similar to adults with complete staging and cytoreduction-omentectomy, hysterectomy, bilateral salpingoohprectomy **if stage 1, can consider preservation of uterus and contralateral ovary	Platin-based chemotherapy	Office visits with monitoring of CA-125 levels every 2–4 months for 2 years, then every 3–6 months for 3 years, and annually for 5 years.

determine subsequent risk stratification, adjuvant therapy, prognosis, and surveillance. In the adult population, ovarian cancer is staged using the International Federation of Gynecology and Obstetrics system, where adenocarcinoma is the most likely histopathological variant. In the pediatric population, epithelial malignancies are exceedingly rare; thus, these staging guidelines were modified by the Children's Oncology Group (COG).[1]

Complete staging per the COG involves collection of peritoneal fluid/washings for cytology and inspection of all peritoneal surfaces, lymph nodes, the omentum, and the contralateral ovary, along with complete resection of the affected intact ovary with the ipsilateral fallopian tube without tumor spill.[1] Furthermore, if any of the above structures are abnormal, then a biopsy should be performed to rule out metastatic disease. This is in contrast to adult women, in which the uterus and contralateral ovary and fallopian tube are typically surgically debulked/removed. Optimal surgical management can be accomplished by a dual effort from both gynecology and pediatric surgery where possible, as pediatric and adolescent gynecologists are not usually trained in surgical staging. If the surgical staging maneuvers are not performed for whatever reason or the tumor is spilled, then the child will be upstaged by definition and could be subject to adjuvant therapy. A brief overview of management can be seen in Table 2.[25]

Once surgery is completed, the specimens are sent to pathology for final histologic diagnosis. It is imperative that the surgical and oncologic providers are in close contact with the pathologists to expedite a final diagnosis, which will guide postoperative therapy and subsequent surveillance (Table 2). After a histologic diagnosis is reached, a multidisciplinary review and discussion will be required to determine what other staging studies are required, if any. Once final staging is completed, the oncology team will manage the delivery of adjuvant therapies and surveillance studies. If chemotherapy is required for treatment, a second discussion with the family and team members regarding fertility preservation should be broached if not already discussed before surgery. If an oncofertility specialist is available, their involvement would be critical at this time. In addition, genetic counseling might also be needed pending the histologic diagnosis and identification of any inherited mutations. Overall, girls with ovarian cancer have a favorable prognosis as most is of germ cell origin, and they have overall survival rates of more than 85% with adjuvant chemotherapy.[1,23–26]

Fertility Considerations

Optimizing fertility is a special concern in the pediatric and adolescent population afflicted with malignant ovarian neoplasms. Issues affecting fertility arise with both the surgical and medical management of these malignancies. Many studies have shown that gynecologists, and in particular pediatric gynecologists, favor fertility-sparing surgery.[2,27] As the field of pediatric and adolescent gynecology grows, our hope is that discussions regarding fertility are addressed early in the course of treatment. In addition, it is well known that certain chemotherapeutic agents are more gonadotoxic than others, and this fact must be acknowledged and recognized by pediatric practitioners.

Platinum-based agents, which are the mainstay chemotherapeutic agent for germ cell malignancies, found most commonly in this population, are the most concerning drug class, but others also exist.[28] If time allows, ovarian tissue extraction and cryopreservation for future fertility should be offered to patients prior to initiation of chemotherapy.[28] Additionally, if a patient is postpubertal with sufficient time available, an oocyte retrieval with cryopreservation should be offered.[29] These ovarian tissue harvest procedures for fertility preservation can be performed in the same operative setting when the vascular access device is placed for chemotherapy. In combining these procedures, the number of anesthetics the child needs is reduced, and the delivery of ongoing, cure-directed care is more efficient.

Once puberty is reached, an additional consideration is the role of ovarian cyst suppression if there remains a healthy ovary. Hormonal methods such as oral contraceptive pills might be offered to suppress cyst formation in a sole remaining ovary to decrease the risk of ovarian torsion and thus loss of ovarian function.

Conclusions

Most ovarian masses in the pediatric and adolescent population are benign, but there still remains a significant risk for malignancy. Depending on the setting and resources available, these patients can be managed by a variety of providers, including but not limited to pediatric and adolescent gynecologists, oncologists, pediatric surgeons, adult gynecologists, and gynecologic oncologists. In addition, radiologists and pathologists play a crucial role in the development of treatment strategies for these patients with suspected and/or confirmed malignancy. Interdisciplinary management is thus imperative for the successful treatment of children and adolescents with malignant ovarian tumors.

References

1. Edited by Mahajan P, Weldon CB, Frazier AL, et al Gynecologic benign and malignant cysts/masses/tumors. In: Emans SJ, Laufer MR, DiVasta AD, editors. Emans, Laufer, & Goldstein's Pediatric and Adolescent Gynecology. Philadelphia, Wolters Kluwer, 2020, pp. 558–69. Edited by.
2. Lawrence AE, Gonzalez DO, Fallat ME, et al: Factors associated with management of pediatric ovarian neoplasms. Pediatrics 2019; 1:144.
3. Zhang M, Jiang W, Li G, et al: Ovarian masses in children and adolescents an analysis of 521 clinical cases. J Pediatr Adolesc Gynecol 2014; 3:27.
4. Peeraully R, Henderson K, Fairbrother K, et al: Effect of surgical specialty on management of adnexal masses in children and adolescents: an 8-year single–center review. J Pediatr Adolesc Gynecol 2020; 1:33.
5. Depoers C, Martin FA, Nyangoh Timoh K, et al: A preoperative scoring system for adnexal mass in children and adolescents to preserve their future fertility. J Pediatr Adolesc Gynecol 2019; 1:32.
6. Oue T, Uehara S, Sasaki T, et al: Treatment and ovarian preservation in children with ovarian tumors. J Pediatr Surg 2015; 12:50.
7. Gonzalez DO, Cooper JN, Aldrink JH, et al: Variability in surgical management of benign ovarian neoplasms in children. J Pediatr Surg 2017; 6:52.
8. Bristow RE, Nugent AC, Zahurak ML, et al: Impact of surgeon specialty on ovarian-conserving surgery in young females with an adnexal mass. J Adolesc Health 2006; 3:39.
9. Eskander RN, Bristow RE, Saenz NC, et al: A retrospective review of the effect of surgeon specialty on the management of 190 benign and malignant pediatric and adolescent adnexal masses. J Pediatr Adolesc Gynecol 2011; 5:24.
10. Childress KJ, Patil NM, Muscal JA, et al: Borderline ovarian tumor in the pediatric and adolescent population: a case series and literature review. J Pediatr Adolesc Gynecol 2018; 1:31.
11. van Heerden J, Tjalma WA: The multidisciplinary approach to ovarian tumours in children and adolescents. Eur J Obstet Gynecol Reprod Biol 2019; 243:243.
12. Callard A, Williams J, Skirton H: Counseling adolescents and the challenges for genetic counselors. J Genet Couns 2012; 4:21.
13. Pichini A, Shuman C, Sappleton K, et al: Experience with genetic counseling: the adolescent perspective. J Genet Couns 2016; 3:25.
14. Epelman M, Chikwava KR, Chauvin N, et al: Imaging of pediatric ovarian neoplasms. Pediatr Radiol 2011; 9:41.
15. Edited by Ward VL, Estroff JA: Radiologic imaging. In: Emans SJ, Laufer MR, DiVasta AD, editors. Emans, Laufer, & Goldstein's Pediatric and Adolescent Gynecology. Philadelphia, Wolters Kluwer, 2020, pp. 575–608. Edited by.
16. Oltmann SC, Fischer A, Barber R, et al: Pediatric ovarian malignancy presenting as ovarian torsion: incidence and relevance. J Pediatr Surg 2010; 1:45.
17. Ameye L, Timmerman D, Valentin L, et al: Clinically oriented three-step strategy for assessment of adnexal pathology. Ultrasound Obstet Gynecol 2012; 5:40.
18. Peces Rama A, Llanos MC, Sánchez Ferrer ML, et al: Simple descriptors and simple rules of the International Ovarian Tumor Analysis (IOTA) Group: a prospective study of combined use for the description of adnexal masses. Eur J Obstet Gynecol Reprod Biol 2015; 195:195.
19. Timmerman D, Van Calster B, Testa A, et al: Predicting the risk of malignancy in adnexal masses based on the Simple Rules from the International Ovarian Tumor Analysis group. Am J Obstet Gynecol 2016; 4:214.
20. Andreotti RF, Timmerman D, Strachowski LM, et al: O-RADS US risk stratification and management system: a consensus guideline from the ACR ovarian-adnexal reporting and data system committee. Radiology 2020; 1:294.
21. Oltmann SC, Garcia N, Barber R, et al: Can we preoperatively risk stratify ovarian masses for malignancy? J Pedatr Surg 2010; 1:45.
22. Rogers EM, Casadiego Cubides G, Lacy J, et al: Preoperative risk stratification of adnexal masses: can we predict the optimal surgical management? J Pediatr Adolesc Gynecol 2014; 3:27.
23. Madenci AL, Levine BS, Laufer MR, et al: Preoperative risk stratification of children with ovarian tumors. J Pediatr Surg 2016; 51:9.
24. Ye G, Xu T, Liu J, et al: The role of preoperative imaging and tumor markers in predicting malignant ovarian masses in children. Pediatr Surg Int 2020; 3:36.
25. Salani R, Khanna N, Frimer M, et al: An update on post-treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncology (SGO) recommendations. Gynecol Oncol 2017; 1:146.
26. Nasioudis D, Ramer I, Sisti G, et al: Risk of second primary tumors after childhood and adolescent ovarian malignancies: a SEER analysis (1973–2011). J Pediatr Adolesc Gynecol 2015; 6:28.
27. Xac MC, Jetelina KK, Jarin J, et al: Benign, borderline, and malignant pediatric adnexal masses: a ten-year review. J Pediatr Adolesc Gynecol 2021; 34. doi:10.1016/j.jpag.2021.01.002.
28. ACOG Committee Opinion No. 747: Gynecologic issues in children and adolescent cancer patients and survivors. Obstet Gynecol 2018; 2:132.
29. Pashankar F, Hale JP, Dang H, et al: Is adjuvant chemotherapy indicated in ovarian immature teratomas? A combined data analysis from the Malignant Germ Cell Tumor International Collaborative. Cancer 2016; 2:122.