“Management of the Adnexal Mass”
James H. Liu, MD, and Kristine M. Zanotti, MD
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Questions written by:
Rini Banerjee Ratan, MD
Department of Obstetrics and Gynecology
New York Presbyterian Hospital
Columbia University College of Physicians and Surgeons
New York, NY

Responses written by:
James H. Liu, MD
Department of Obstetrics and Gynecology

Kristine M. Zanotti, MD
Department of Obstetrics and Gynecology,
Division of Gynecologic Oncology

UH MacDonald Womens Hospital,
Case Medical Center
Cleveland, OH

1. You mention that three-dimensional ultrasonography may be more accurate than two-dimensional ultrasonography in identifying adnexal masses that may be malignant. What are your criteria for obtaining a three-dimensional sonogram? You also note that magnetic resonance imaging (MRI) is more specific than two-dimensional ultrasonography in identifying malignant adnexal masses. Do you recommend obtaining an MRI from all women prior to referral to a gynecologic oncologist, or prior to undertaking surgery?

Response from Drs. Liu and Zanotti
To justify its additional cost, the most appropriate use for three-dimensional ultrasonography or MRI is for patients with an adnexal mass found by two-dimensional imaging, where the mass is of indeterminate or intermediate risk for malignancy and a decision for operative versus nonoperative intervention could be influenced by a test with improved test characteristics. Two-dimensional ultrasonography is sensitive enough to identify adnexal masses, but is less able than MRI or three-dimensional ultrasonography to be used to exclude malignancy among those with an adnexal mass. Unless deemed useful to determine surgical approach, these tests need not be obtained in situations where the decision for surgery can be made based on two-dimensional imaging alone, such as with the symptomatic patient or one at higher risk for malignancy.
2. Is there ever a role for obtaining a CA 125 level in a premenopausal patient with a complex adnexal mass?

Response from Drs. Liu and Zanotti
The low specificity of CA125 in general and in the premenopausal patient specifically limits its usefulness in the management of premenopausal patients at otherwise relatively low risk for malignancy. False positive rates dwarf true positive rates and are too high to justify their routine use in the premenopausal patient. However, positive predictive value is improved in higher-risk (higher-prevalence) situations, such as masses of increasing size and complexity, or in the presence of other significant clinical risk factors, and may provide useful information in these settings.

3. Many patients do their own “research” on the Internet before coming to see their physician. If a woman is found to have an adnexal mass, is undecided about surgery, and requests serum-based proteomic testing to better delineate her risk of malignancy, should the multivariate index assay (OVA1 test) be performed upon her request? Will commercial insurance carriers be likely to cover the cost?

Response from Drs. Liu and Zanotti
Currently, the OVA1 test is indicated for women with an adnexal mass for whom surgery is planned to further assess the likelihood of the mass’s benignancy or malignancy. The test’s clinical usefulness is in surgical planning and determining the appropriateness of referral to a gynecologic oncologist. Medicare announced in March 2010 that it will begin covering OVA1, although insurance reimbursements are not universal.

4. You state that surgical exploration is typically performed for adnexal masses that are highly suspicious for cancer. Given the increasing popularity and widespread marketing of robotic surgical procedures, is there a role for robotic surgery in the management of high-risk adnexal masses?

Response from Drs. Liu and Zanotti
While surgeons are exploring the potential role of robotic surgery for highly selected cases of ovarian cancer, at this time there are insufficient comparative outcomes data to advise its use in women at high risk for ovarian cancer.
5. In postmenopausal patients who undergo surgery for an adnexal mass, is there any benefit to preserving a normal-appearing contralateral ovary?

Response from Drs. Liu and Zanotti

While cardiovascular disease, hip fractures, and all-cause mortality are increased in premenopausal women undergoing bilateral oophorectomy for benign disease, published studies in the postmenopausal patient are conflicting. However, a recent publication from the Women’s Health Initiative, a prospective observational study of over 25,000 postmenopausal women aged 50–79 years, the risk of cardiovascular disease, stroke, hip fracture, and death were similar in women undergoing bilateral oophorectomy versus those who did not. Moreover, the risk of ovarian cancer was reduced by less than 1% in women, with no significant effect on rates of breast, colorectal, or lung cancer.¹

6. What is the role of prophylactic salpingo-oophorectomy in women with a known BRCA1 or BRCA2 genetic mutation? Is there an age at which you routinely recommend prophylactic salpingo-oophorectomy? If so, how do you counsel these patients regarding the risks and benefits of subsequent hormone replacement therapy?

Response from Drs. Liu and Zanotti

Risk-reducing salpingo-oophorectomy is the most effective measure for cancer risk reduction in BRCA mutation carriers and is recommended by the National Comprehensive Cancer Network (NCCN).² In addition to the demonstrated dramatic reduction in ovarian, fallopian tube, and primary peritoneal cancer risk, a substantial reduction in breast cancer is also seen among premenopausal women choosing the procedure. Moreover, younger patients benefit proportionately more than older patients with respect to breast cancer risk reduction.

Ideally, the risk-reducing salpingo-oophorectomy is performed earlier than the ages at which an increase in risk for ovarian cancer is observed (late 30s and early 40s for BRCA1 carriers, and 10 years later for BRCA2 carriers). Moreover, when counseling individual patients regarding the timing of this procedure, one must also balance considerations for a desired effect on breast cancer risk reduction with personal childbearing wishes and quality of life and health concerns related to early menopause. Counseling patients in this regard can be complex. Short-term hormone replacement may not necessarily undermine the protective effect of salpingo-oophorectomy among BRCA1 and BRCA2 mutation carriers, but long-term use may carry increased breast cancer risk.
7. Women who are known carriers of *BRCA1*, *BRCA2*, or *HNPCC* genetic mutations often have an understandably high degree of concern and anxiety regarding their increased risk of developing ovarian cancer. What screening regimen or protocol do you recommend for women who are at high risk for hereditary ovarian cancer?

**Response from Drs. Liu and Zanotti**

*The National Comprehensive Cancer Network (NCCN) Guidelines recommend risk-reducing oophorectomy and state, “For those patients who have not elected risk-reducing salpingooophorectomy, consideration can be made to concurrent transvaginal ultrasonography + CA-125 every 6 months starting at age 35 years old or 5–10 years before the earliest age of first diagnosis of ovarian cancer in the family.”* Unfortunately, it is acknowledged by the NCCN that such screening has not yet demonstrated associated reductions in ovarian cancer related deaths, even in a high-risk population. Moreover, it is not clear that such screening reduces anxiety in this setting.

Anxiety of varying degrees is a near-universal finding among women who are carriers of *BRCA1*, *BRCA2*, or *HNPCC* genetic mutations, and addressing this anxiety is an important component of treating these patients. While a program of ovarian screening may lend assurance to some women, it is very common for such a program to cause increased anxiety, further complicated by a high rate of false positive results. The Gynecologic Oncology Group is currently prospectively investigating a broad variety of health-related outcomes in women at high risk who elect either twice yearly screening or risk-reducing salpingooophorectomy. Psychometric assessments are among the many outcomes measured in this important comparative study, which is anticipated to be completed within the year.

8. Do you recommend that frozen section pathology be obtained for all patients undergoing surgery for an intermediate-risk or high-risk adnexal mass?

**Response from Drs. Liu and Zanotti**

Frozen section should be obtained for any case in which intraoperative decisions would be influenced by the results of the pathologic findings. This is often the case when malignancy is on the differential diagnosis. However, diagnosis can sometimes be determined intraoperatively through gross inspection only.
9. Under what circumstances do you recommend oophorectomy compared with ovarian cystectomy in a pediatric patient undergoing surgery for an adnexal mass? Should pediatric patients or young women with early stage ovarian malignancies be offered oocyte or ovarian tissue cryopreservation?

Response from Drs. Liu and Zanotti

Ovarian pathology is a relatively rare indication for surgery in girls and women less than 20 years of age. When ovarian pathology is identified, rigorous preoperative assessment and planning is essential to identify the most appropriate care in the pediatric and young adult population undergoing surgery for an adnexal mass.

Although most ovarian masses in the pediatric and young adult population are benign, a subset of patients will have malignant tumors, and a subset of those tumors may be very aggressive. Because most of these lesions are benign, ovarian-preserving operations such as cystectomy should be performed whenever feasible. If a malignancy is identified and ovarian pathology is unilateral, as is often the case in this population, then unilateral oophorectomy is most appropriate. Thus, oocyte or ovarian tissue cryopreservation technology will not be needed in most cases. However, multiagent chemotherapy may result in ovarian failure in approximately 40% of women less than 40 years of age. Thus, if the anticipated ovarian pathology is aggressive and one in which extensive multiagent adjuvant chemotherapy will be recommended postoperatively, then oocyte cryopreservation may be a reasonable option.

10. Are any promising new techniques being developed for the early detection of Type I epithelial ovarian cancers?

Response from Drs. Liu and Zanotti

Because of its relative rarity and propensity for very early dissemination, detection of early stage Type I epithelial ovarian cancer in the general population has been a challenge. A variety of potential biomarkers have been identified and evaluated alone, as part of a panel of multiple biomarkers, and in combination with transvaginal ultrasonography. Although a multitude of studies are ongoing, to date prospective studies have yet to validate any screening strategy or technology with sufficient sensitivity and specificity to recommend for the general population.
References:
