Laparoscopic Management of Adnexal Masses

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The discovery of an adnexal mass is a common clinical problem affecting women of all ages. From 5% to 10% of American women will undergo a surgical procedure in their lifetime owing to a suspected ovarian neoplasm and between 13% and 21% of these women will be diagnosed with ovarian cancer.[1]

Thus, although the majority of adnexal masses are benign, the primary goal of diagnostic evaluation is the exclusion of malignancy. Currently, there is no effective way to screen for ovarian malignancy, and the risk rises with increasing age. Ovarian cancer is the leading cause of death from gynecologic cancers and the fifth leading cause of cancer death in women in the United States, with 15,280 deaths annually and a 1.42% lifetime risk of dying from ovarian malignancy.[2,3] The poor rates of survival result from a lack of early warning signals, sensitive screening, or early detection techniques.[4]

Some women with adnexal masses may present with acute torsion or rupture and peritoneal signs requiring immediate surgical intervention; however, the vast majority of adnexal masses are discovered incidentally during imaging or on pelvic exam.[1,5] Adnexal masses discovered incidentally represent a diagnostic and management dilemma.

This review will detail recent advances in diagnosis, treatment, and, importantly, minimally invasive surgical techniques that have the potential to decrease unnecessary morbidity among patients during evaluation of adnexal masses.

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DIAGNOSIS

Most adnexal masses arise from the ovary. Nevertheless, the differential diagnosis for any adnexal mass includes differentiation between an "extraovarian mass" (ectopic pregnancy, tuboovarian abscess, peritoneal inclusion cyst, pedunculated fibroid, diverticular abscess, appendiceal abscess/tumor, fallopian tube cancer, inflammatory/malignant bowel disease, and pelvic kidney) and an "ovarian mass" (physiologic cysts, endometrioma, theca lutein cysts, primary neoplasms, and metastatic carcinoma).[6]

The diagnostic evaluation of a woman with an adnexal mass begins with a thorough history and physical examination. Imaging, with or without laboratory studies, is necessary in a majority of cases. The ultimate diagnostic tool is histological examination.[6,7]

History

Special attention should be paid to the patient's family history, characteristics of her pain, and her menstrual history. It has been shown that more severe or more frequent than expected symptoms of recent onset warrant further diagnostic investigation because they are more likely to be associated with malignant ovarian masses.[8] Nulliparity, history of infertility and/or endometriosis, and a family history of breast, ovarian, or colon cancer are considered risk factors for ovarian cancer.[6,9,10] It has also been shown in recent studies that postmenopausal women who use hormone replacement therapy (HRT) are at an increased risk of ovarian cancer.[11–13]

The most important decision point in assessment of malignant potential for an adnexal mass is the stage of a woman's reproductive life. The suspicion for a malignancy is increased in prepubescent (germ cell tumors) and postmenopausal women (epithelial ovarian cancer) while masses in menstruating women are more likely to be gynecologic and most are functional cysts. Postmenopausal patients with adnexal masses undergoing surgical evaluation have an 8% to 45% chance of malignancy, while malignancy has been found in only 7% to 13% of premenopausal women undergoing similar procedures.[14,15] Nulliparous patients have been shown to have a 2- to 3-fold increased risk of ovarian cancer as compared with parous women. Endometriosis has been associated with increased risk of ovarian cancer and malignant transformation has been demonstrated.[16] Among familial risks, approximately 5% to 10% of epithelial ovarian cancers are suspected to be genetically based, a majority of which include *BRCA1* and *BRCA2* mutations.[1,17]

Physical Examination

The bimanual and rectovaginal examination focus on the size, location, consistency, and mobility of the adnexal mass to help formulate a differential diagnosis. However, these examinations, even when performed in conjunction with a rectal exam and even when performed under anesthesia, have limited utility both for detection and differentiation of an adnexal mass. Detection rates as low as 60% have been reported.[18] The bimanual exam is limited by body habitus and thus detection rates presumably are hampered even further by obesity.[19]

Imaging

Multiple imaging modalities are used in the diagnosis and the differentiation of adnexal masses including ultrasound, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomographic (PET) scanning. Transvaginal sonography has emerged as the imaging modality of choice given its widespread

availability, tolerability for the patient, and cost-effectiveness.[1,20] A complete ultrasound assessment will include both a transvaginal and an abdominal component so as to fully characterize masses that may be both pelvic and abdominal. The report should include the size and consistency of the mass (cystic, solid, mixed); its location (ovarian, uterine, bowel); whether unilateral versus bilateral; and the presence or absence of certain characteristics that may help determine an individual's risk of malignancy. Characteristics of ovarian cysts that are generally associated with a higher risk for malignancy include increasing size over multiple imaging studies, septations, excrescences, mural nodules, papillary projections, solid components, and the presence of ascites.[21,22] Color Doppler ultrasonography and 3-dimensional sonography with "vascular sampling" of suspicious areas have also been investigated, but further studies are required to fully delineate their utility. Scoring systems, such as the Pelvic Mass Score (PMS) suggested by Rossi and colleagues, and the Risk of Malignancy Index (RMI), can be used to determine the likelihood of malignancy.[23–25] A meta-analysis of various scoring systems revealed a pooled sensitivity and specificity ranging from 86% to 91% and from 68% to 83%, respectively.[1]

Typical findings for certain benign adnexal masses have been described in smaller studies. Endometriomas will consist of a round homogeneous fluid filled mass with low-level echoes.[26,27] Mature teratomas will contain hypoechoic components and multiple small homogeneous interfaces.[28] Hydrosalpinges appear as tubular sonolucent cysts.[29]

Incidental adnexal masses are sometimes found during CT scans for other indications. As with ultrasonography, a CT scan can help identify the size, location, and relationship of the adnexal mass to other organs. However, a CT scan is a less reliable imaging modality compared to ultrasonography and cannot as easily demonstrate the internal characteristics of adnexal masses. CT scans are most useful for assessing the remainder of the abdomen and pelvis when metastatic disease is suspected. By contrast, in select cases when ultrasonographic findings are uncertain, MRI can help further characterize the adnexal mass.[30] MRI is particularly useful in differentiating the origin of nonadnexal pelvic masses. With each of these imaging modalities, certain characteristics can shed clues as to the etiology of the mass (**Table 1**).[30] There is no current role for PET scan in the evaluation of adnexal masses.

Routine screening for ovarian cancer is not currently recommended by any medical organization.[31,32] However, large-scale studies over recent years have demonstrated the feasibility and potential of multimodal screening strategies.[33–35] Given the low prevalence of ovarian cancer in the general population, any successful screening strategy must have both high specificity and sensitivity; in one review, values of greater than 75% and 99.6%, respectively, were suggested.[36] Early reports from the UK Collaborative Trial of Ovarian Cancer Screening have shown that a multimodal approach to screening involving yearly CA-125 with second-line transvaginal ultrasounds has the highest sensitivity (89.4%) and specificity (99.8%).[34] Investigations will continue to determine the optimal screening method, and novel biomarkers likely will serve to increase both sensitivity and specificity in this important preventative measure.

Laboratory Studies

Laboratory tests used during the evaluation of an adnexal mass should include serum markers, complete blood count, serum electrolytes, urinalysis, and fecal occult blood test.

Table 1
Classification of Adnexal masses by imaging features

	No or Few Solid Elements	Some Solid Elements
Cystic Tumors		
Containing serous fluid	Serous cystadenoma	Borderline serous tumor Serous adenofibroma
Containing mucinous fluid	Mucinous cystadenoma	Borderline mucinous tumor Mucinous adenofibroma
Containing blood	Corpus luteum cyst Endometriotic cyst Benign cyst with secondary hemorrhage	Borderline endometrioid tumor Endometrioid adenofibroma Borderline cyst with secondary hemorrhage
Containing lipid	Teratoma (ie, dermoid cyst)	Teratoma (ie, dermoid cyst)
Predominantly Solid Tumors		
Epithelial		
Serous cystadenocarcinoma		
Mucinous cystadenocarcinoma		
Endometrioid cystadenocarcinoma		
Clear cell cystadenocarcinoma		
Brenner tumor: benign, borderline, or malignant		
Germ cell and sex cord stromal		
Granulosa cell tumor		
Thecoma and other sex cord stromal tumors		
Teratoma (ie, dermoid cyst)		
Dysgerminoma		
Yolk sac tumor		
Other		
Fibroma		
Lymphoma		
Metastatic tumors		

Data from Bharwani N, Reznek RH, Rockall AG. Ovarian cancer management: the role of imaging and diagnostic challenges. Eur J Radiol 2011;78:41–51.

CA-125 is a serum marker that is elevated in approximately 80% of women with ovarian cancer. However, although CA-125 is elevated in 90% of women with advanced disease, it is elevated in only 50% of women with stage I disease at the time of diagnosis.[1,2] In addition, CA-125 is a nonspecific marker that can be elevated in many other conditions, including other malignancies such as endometrial cancer and certain pancreatic cancers; benign gynecologic etiologies such as endometriosis, uterine fibroids, and pregnancy; nongynecologic conditions such as gastroenteritis, pancreatitis, cirrhosis, congestive heart failure, liver failure, pleuritis, pneumonia, or pleural effusion of any origin; and in approximately 1% of healthy patients.[6,37] Thus, CA-125 has both poor sensitivity and poor specificity as a screening test for ovarian cancer. Serum CA-125 levels have been demonstrated to be more accurate among a postmenopausal population with a positive predictive value of 98% and a negative predictive value of 72%. In contrast, in premenopausal patients CA-125 levels have a positive predictive value of only 49%.[38] In recent biomarker studies, combined testing of CA-125 and human epididymis 4 (HE4) provided the greatest level of discrimination between adnexal masses that were benign versus malignant.[39] However, combining the markers HE4 and CA-125 does not seem to lead to more accurate detection rates of ovarian malignancy.[40]

Serum human chorionic gonadotropin (hCG) should be obtained in women of reproductive age to rule out pregnancy and, along with other serum markers such as alpha-fetoprotein (AFP) and lactate dehydrogenase (LDH), can be helpful in young women when a germ cell tumor is suspected. Obtaining estradiol, dehydroepiandrosterone (DHEA), and testosterone levels may be helpful in women suggested to have functional tumors, such as steroid tumors, or if a girl younger than 12 years is being evaluated.

TREATMENT

The primary goal in the evaluation and the treatment of an adnexal mass at any age is to rule out ovarian malignancy. The suspicion for a malignancy is increased in prepubescent (germ cell tumors) and postmenopausal women (epithelial ovarian cancer).

Medical Therapy

Asymptomatic, small, well-characterized adnexal masses may be observed with regular pelvic examinations and radiologic evaluations in premenopausal women. A recent study supports following simple unilocular ovarian cysts in postmenopausal women without intervention.[41] The American College of Obstetrics and Gynecology notes that simple cysts up to 10 cm in diameter are almost universally benign and can be safely followed without intervention, even in postmenopausal patients.[1] Although hormonal contraceptives are often prescribed to suppress ovarian cysts, reviews have concluded that functional cysts will not regress more quickly with estrogen-progestin contraceptive therapy when compared to expectant management.[42] Adnexal masses detected incidentally during routine sonography in pregnancy can also be followed expectantly. The majority are physiologic or benign tumors that will resolve spontaneously.

A surgical approach should be used if growth occurs in these masses, if the patient becomes symptomatic, or if the mass develops more concerning features, such as solid components or papillary projections. Persistant adnexal masses at extremes of age—pubertal and postmenopausal—should be evaluated surgically as the suspicion for malignancy is high. Postmenopausal patients with adnexal masses undergoing surgical evaluation may have up to a 45% chance of malignancy.[14]

Surgical Therapy

Women with cysts larger than 10 cm and those with findings suspicious for malignancy require surgical exploration. In addition to the cyst's sonographic appearance, findings suspicious for malignancy include no change or an increase in size, a highly elevated CA-125 (>200 U/mL), ascites, suspicion of metastatic disease, or a positive family history.[43] Similar studies indicate that a surgical approach should be used if growth occurs in these masses, if the patient becomes symptomatic, or if the mass develops more concerning features, such as solid components or papillary projections.

The traditional surgical approach to adnexal masses has been via laparotomy. However, regardless of the index of suspicion for malignancy, laparoscopic evaluation of adnexal masses is appropriate in the hands of a skilled laparoscopic surgeon. The sequence of events should parallel those implemented in laparotomy: a thorough evaluation of the abdomen and pelvis, peritoneal washings, cystectomy or adnexectomy as indicated, biopsies of suspicious lesions, and frozen section evaluation. **Fig. 1** demonstrates findings on laparoscopy that are concerning for malignancy. The incidence of unsuspected malignancy ranges from 0.4% to 14% in patients undergoing laparoscopic evaluation for adnexal masses.[44]

Surgical therapy for benign appearing lesions

Ovarian cysts. Our group has previously described optimal laparoscopic management of benign ovarian cysts.[45] The major benefit of the laparoscopic approach in the management of any adnexal mass and especially in instances of benign disease is the avoidance of overtreatment and unnecessary laparotomy.

Surgical treatment of benign appearing cyst must follow the protocol described here including cytologic examination of pelvic washings and frozen section. Cyst aspiration alone is not recommended. The pathologic examination of cyst fluid is not adequate to assess for malignancy. From 10% to 65% of cyst aspirates will be interpreted as benign when in fact malignancy is present. Moreover, cyst recurrence is common with simple aspiration.[45]

An ideal ovarian cystectomy will consist of removal of the cyst intact with limited trauma to residual ovarian tissues. With larger cysts, aspiration is appropriate so as to decompress the mass and assist in dissection and excision. If the cyst ruptures, the resulting contamination is greater than if the cyst were opened and aspirated.[45] Methods for aspiration of larger cysts have previously been described.[45] However, teratomas should be removed intact whenever possible. Laparoscopic management of dermoid cysts was reported as early as 1987.[46–49]

Removal of the cyst wall is essential to prevent recurrence. If the cyst wall cannot be identified, the edge of the ovarian incision can be "freshened" with scissors to reveal a clean edge and assist dissection. A key step in complete excision of a cyst and its wall, whether assisted by aspiration or not, is the atraumatic development of the correct plane between the wall and ovarian tissues. This can be more easily accomplished with the use of hydrodissection. An 18- or 20-gauge needle is introduced through an accessory trocar sleeve. Alternatively, a 7.5-in spinal needle can be introduced through the abdominal wall. Dilute vasopressin is injected between the capsule and ovarian cortex creating a plane that is subsequently developed using the suction-irrigator as a blunt probe. After complete removal of the cyst and capsule, the base is irrigated and hemostasis is ensured using the CO_2 laser or bipolar electrocoagulation. If the ovarian edges overlap well, no further repair is necessary. However, in some instances, fine absorbable microfilament suture can be used to bring the

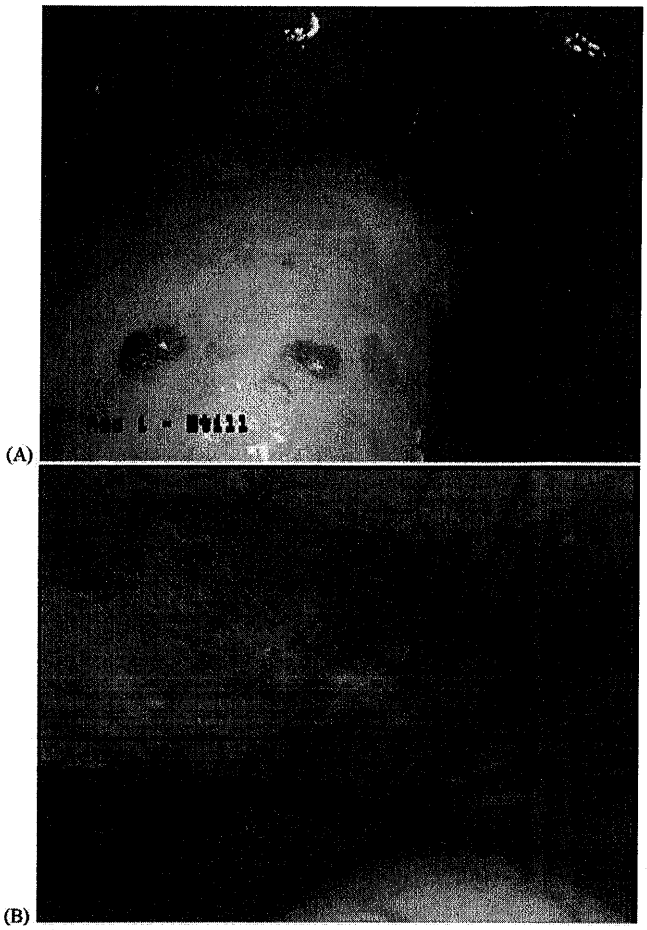

Fig. 1. Suspicious adnexal mass. *(A)* Surface ovarian excrescences positive for malignant implants. *(B)* Metastatic implants visualized during laparoscopic survey in the upper abdomen and anterior abdominal wall.

edges together and promote healing. The sutures should be buried inside the ovary to prevent formation of adhesions.[45]

Excised tissues should be removed with the assist of a specimen removal bag. Methods to aid in removal have been previously described and include further cyst aspiration, morcellation, and decreasing the pneumoperitoneum.[45] The surgeon must ensure that all tissue is removed and that contamination of the anterior abdominal wall does not occur as this can lead to ovarian remnant.

If contamination does occur, for example, if the specimen removal bag ruptures, all efforts must be made to remove all tissue and the incision must be copiously irrigated.

Ovarian remnant. Ovarian remnant syndrome (ORS) is defined as the persistence of functional ovarian tissues after oophorectomy. Laparoscopic management of ovarian remnants was reported as early as 1992.[50,51]

Most women with ORS present with chronic pelvic pain, dyspareunia, and postcoital pain. ORS results from incomplete excision of ovarian tissues at the time of bilateral oophorectomy. A variety of risk factors predispose to this condition and include extensive adhesive disease from endometriosis, pelvic inflammatory disease, inflammatory bowel disease, appendicitis or appendectomy, a history of previous surgeries, and neoplastic lesions.[51]

The sonographic appearance of ovarian remnants varies from small to large and includes both cystic or multiseptated masses with some component of vascularized ovarian tissue. ORS is more likely to occur on the left side because the infundibulopelvic ligament on this side is partially obscured by its relationship to the sigmoid colon and appears shorter leading to incomplete excision.[52] Low or borderline levels of follicle-stimulating hormone in patients with documented bilateral oophorectomy are consistent with the presence of retained ovarian tissue. Clomiphene citrate or human menopausal gonadotropin can be used to increase the remnant's size to aid in the diagnosis preoperatively or to assist in locating the tissue at the time of surgery if extensive adhesions are suspected.

Patients with ORS will have a prior surgical history and the chance of adhesive disease, including anterior abdominal wall adhesions, is likely; thus, an open entry or mapping technique is advised.[51] The surgeon should proceed with extensive and careful retroperitoneal dissection to facilitate identification and removal of all ovarian tissue.

Laparoscopic management of ORS is feasible and safe in the hands of experienced surgeons. Despite objections to the use of minimally invasive approaches in ORS,[53] case series have reported excellent outcomes after laparoscopic management.[50,54–56]

Surgical therapy for probable malignancy

When an obvious epithelial ovarian malignancy is encountered, a complete staging protocol must be performed. This includes complete exploration of the abdomen, total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and paraaortic lymph node dissections, biopsies of the undersurface of the right and left diaphragms, and biopsies of the colic gutters followed by a maximal resection of the intra-abdominal tumor. In select cases involving women with limited, early stage, low-grade ovarian cancers, a fertility-sparing procedure may be considered. When malignancy has spread to the abdominopelvic cavity, cytoreduction to minimal or preferably no disease should be performed.

Borderline (low malignant potential) tumors

Borderline ovarian tumors represent 10% to 20% of epithelial ovarian cancers and typically have an excellent prognosis. Survival rates for all borderline ovarian tumors range from 92% among those with advanced stage disease to 98% in those with stage I disease.[57] Borderline ovarian tumors occur predominantly in a premenopausal population with the highest frequency occurring in patients aged 30 to 50; 50% to 85% of these are diagnosed as stage I. The 2 most frequent histologic subtypes of borderline ovarian tumors are serous and mucinous tumors. Serous tumors are bilateral in 30% of cases with concurrent peritoneal implants in 35% of cases.[57] Mucinous tumors are malignant in only 5% of cases with rare case reports of nodal metastases; thus, complete staging may not be necessary in these cases. Appendiceal primaries are quite common among the mucinous tumors, so appendectomy is routinely performed.

Fertility-sparing options in reproductive age patients range from cystectomy to adnexectomy. Recurrence rates vary depending on the surgical approach: adnexectomy

recurrence rates range from 0% to 20%, and cystectomy recurrence rates range from 23% to 58%.[57] Laparoscopically assisted hysterectomy for the management of a borderline ovarian tumor was reported in 1992.[58] Since then, laparoscopic staging in borderline ovarian tumors has become increasingly common with advances in endoscopic techniques and instruments.[59]

Early stage invasive ovarian cancer

Early stage invasive ovarian cancer requires complete surgical staging to obtain important prognostic information, to avoid understaging of patients, and to determine the optimal postoperative management. Staging typically includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, peritoneal biopsies, pelvic and para-aortic lymph node dissection, and peritoneal washings. While, traditionally, staging of early ovarian cancer had been performed via laparotomy, there is evidence that, in hands of an experienced laparoscopic surgeon, staging of early ovarian cancer is comparably safe and efficient with similar long-term outcomes.

Advances in laparoscopic management of ovarian malignancy would not have been possible without multiple advances in instrumentation and the introduction of videolaparoscopy.[60–62] Before the introduction of videolaparoscopy, the utility of operative laparoscopy was diminished by two major drawbacks: poor visualization into the intra-abdominal cavity with one eye and the inability of the operative team to view the operative field. Both of these limitations were rectified with the incorporation of the videolaparoscope.[62,63] These advances made it possible to treat even the most extensive pathology laparoscopy.[64–66]

Large case-control series were conducted in 2005 through 2008 confirming the comparable efficacy of open and laparoscopic approaches to ovarian cancer staging. Childers and coworkers suggested that laparoscopy may offer an advantage in the management of early ovarian cancer by allowing better visualization of the subdiaphragmatic areas, the obturator spaces, the anterior and posterior cul-de-sacs, as well as magnification and consequent detection of smaller lesions that may be missed on laparotomy.[67] One of the first implementations of laparoscopy was reported by Bagley and colleagues, who described visualization of diaphragmatic metastases that had been missed at the time of laparotomy.[68] The safety of a laparoscopic approach is also suggested in several studies with outcomes rivaling those reported in the literature for laparotomy. Nezhat and coworkers reported laparoscopic treatment and staging of early ovarian cancer in a case series of 36 patients with the longest recorded mean follow-up to date.[69] The mean number of peritoneal biopsies, paraaortic nodes, and pelvic nodes were 6, 12.2, and 14.8, respectively. The mean duration of follow-up was 55.9 months, and there was a demonstrated 100% overall survival rate with no recurrence.

Advanced stage invasive and recurrent ovarian cancer

A majority of patients with epithelial ovarian cancer are diagnosed with either International Federation of Gynecology and Obstetrics (FIGO) stage III or IV disease. The mainstay of treatment includes optimal surgical cytoreduction followed by platinum-based combination chemotherapy. Clinical risk factors that contribute to poor prognosis include FIGO stage IV disease, residual tumor, greater than 20 residual lesions, more than 1 L of ascites, poor performance status, older age, poor histology, high tumor grade, and high postoperative CA-125 levels. Complete surgical staging and/or debulking includes total abdominal hysterectomy, bilateral salpingo-ophorectomy, omentectomy, pelvic and paraoartic lymphadencectomy, and radical resection of all visible disease. In some cases, resecting portions of the small bowel

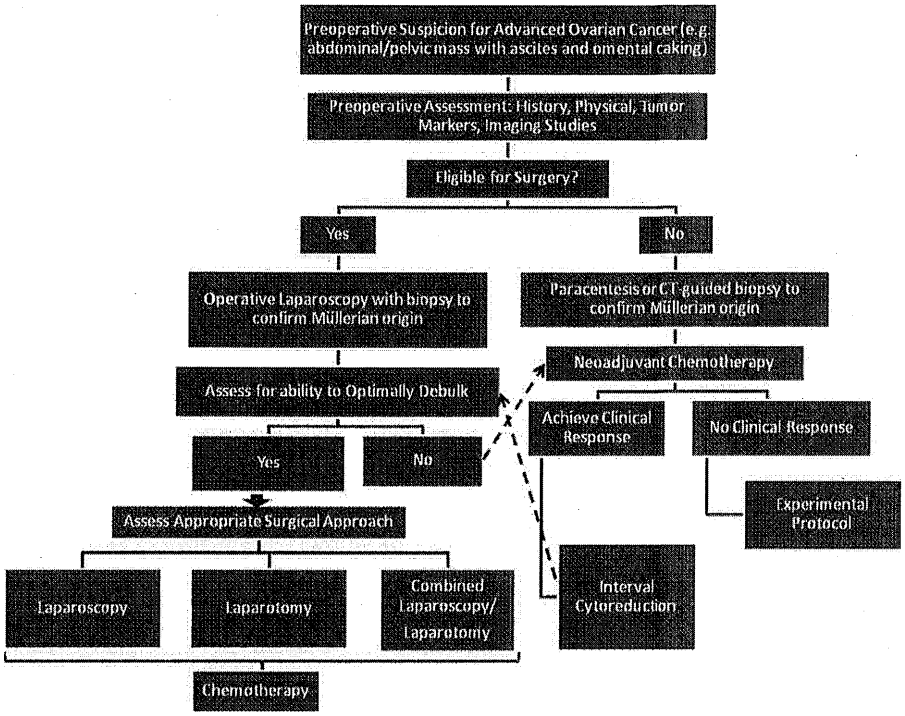

Fig. 2. Protocol for laparoscopic management in advanced ovarian cancer.

or colon may be necessary; therefore, preoperative bowel preparation may be warranted, as is a discussion during the informed consent process about possible bowel resection and diverting colostomy.

Laparoscopy can be used to effectively treat ovarian, primary peritoneal, and fallopian tube malignancies. As the use of laparoscopy has increased in gynecologic oncology, several applications have emerged in the literature: as a triage tool for resectability, as a method for second look evaluation and as a mode to select cases for primary or recurrent cytoreduction.[5] An algorithm, such as the one illustrated in **Fig. 2**, is useful in the management of presumed advanced ovarian cancer given modern technology and appropriate surgical ability. A patient can be optimally debulked to no macrosomic disease, as several studies have demonstrated.[70–72] Laparoscopy can be an ideal mode to assess the patient for suitability for cytoreduction as well. If the patient cannot be debulked, she can receive neoadjuvant chemotherapy. Receiving initial chemotherapy does not necessarily compromise the survival rate, as shown in a recent study by Vergote and colleagues.[73] In fact, chemotherapy can lead to significant tumor reduction making the patient a candidate for successful interval cytoreduction. The patient can then undergo cytoreductive surgery laparoscopically or via laparotomy depending on her unique situation.

Amara and colleagues first reported a small case series that included complete laparoscopic management of advanced or recurrent ovarian cancer.[70] All patients did well postoperatively. One patient died due to recurrent disease after declining further intervention. Nezhat and coworkers published a case series of 32 patients with

advanced ovarian cancer and demonstrated that a complete debulking procedure can be performed laparoscopically in advanced cases.[71] Seventeen patients underwent laparoscopic procedures, while 11 patients underwent laparotomy. The estimated blood loss and hospital stay were not different between the 2 groups. The median time to recurrence was 31.7 months in the laparoscopy group and 21.5 months in the laparotomy group. These data illustrate that laparoscopy is a technically feasible approach in surgical management in selected patients with advanced ovarian malignancy without compromising survival.

Recent publications have explored the role of robotic procedures in the management of ovarian malignancy. Magrina and colleagues looked at perioperative and survival results in woman with ovarian cancer who underwent laparoscopic, robotic, and laparotomy procedures for management of their malignancy. They concluded that the laparoscopic and robotic approaches were preferred in patients requiring primary tumor excision alone or in addition to one additional major procedure. By contrast, laparotomy was preferred in patients with major disease requiring 2 or more additional procedures. Survival was not affected by the approach.[72]

SUMMARY

With the continued expansion of endoscopic techniques and instruments, laparoscopy and minimally invasive techniques are quickly emerging as a feasible alternative to laparotomy in managing adnexal masses and ovarian cancer. Laparoscopy has the potential to completely and successfully treat both benign and malignant adnexal pathology while decreasing unnecessary morbidity among patients. Further advances in technology, techniques, and instruments can only increase this potential.

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