Initial Evaluation and Referral Guidelines for Management of Pelvic/Ovarian Masses

Abstract

Objectives: To optimize the management of adnexal masses and to assist primary care physicians and gynaecologists determine which patients presenting with an ovarian mass with a significant risk of malignancy should be considered for gynaecologic oncology referral and management.

Options: Laparoscopic evaluation, comprehensive surgical staging for early ovarian cancer, or tumour debulking for advanced stage ovarian cancer.

Outcomes: To optimize conservative versus operative management of women with possible ovarian malignancy and to optimize the involvement of gynaecologic oncologists in planning and delivery of treatment.

Evidence: Published literature was retrieved through searches of PubMed or MEDLINE, CINAHL, and the Cochrane Library, using appropriate controlled vocabulary and key words. Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. Grey (unpublished) literature was identified by searching the web sites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Recommendations

1. Primary care physicians and gynaecologists should always consider the possibility of an underlying ovarian cancer in patients in any age group who present with an adnexal mass with a significant risk of malignancy. (II-2B)

2. Appropriate workup of a perimenopausal or postmenopausal woman presenting with an adnexal mass should include evaluation of symptoms and signs suggestive of malignancy, such as persistent pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, and difficulty eating. In addition, CA125 measurement should be considered. (II-2B)
INTRODUCTION

Ovarian cancer is relatively uncommon, yet it is the deadliest of all gynaecologic malignancies, often affecting perimenopausal and postmenopausal women. According to the Canadian Cancer Society statistics, there were 2300 new cases and 1600 deaths due to ovarian cancer in 2006. In the same report, the estimated five-year survival rate for patients with ovarian cancer (1995–1997) was 38% (95% CI 37%–40%). This rate has not changed significantly over the past few decades despite significant advances in surgical techniques, chemotherapeutic options, and supportive care that have, however, improved the median survival.

Standard management for patients with tumour clinically localized to the ovary(ies) includes comprehensive surgical staging to guide subsequent need for further adjuvant treatment and to provide prognostic information. For patients with metastatic disease, numerous retrospective and prospective studies have shown that the extent of residual disease after radical surgical debulking is a significant predictor of both progression-free and overall survival. More recently, intraperitoneal chemotherapy has shown significant survival benefits over standard intravenous chemotherapy in metastatic disease that has been optimally debulked at time of initial surgical exploration, confirming the importance of aggressive surgical tumour resection at the time of initial diagnosis.

A number of case series have shown that patients with ovarian cancer whose initial surgery is performed by gynaecologic oncologists are more likely to be appropriately staged and optimally debulked than those managed initially by general gynaecologists and general surgeons. Despite this, data from a large population-based study suggested that only approximately one third of patients with ovarian cancer were initially managed by gynaecologic oncologists. Likely this is secondary to human resource constraints as well as to the challenges facing physicians in diagnosing cancer preoperatively so appropriate referrals can be made. This guideline is meant to assist physicians in the identification of patients with increased likelihood of underlying malignancy so appropriate referrals can be made to optimize patients’ outcomes in the context of the current Canadian health care system.

OVARIAN MASS INITIAL ASSESSMENTS

Ovarian cancer often remains asymptomatic in its early phase because of the anatomic location of the ovaries deep...
in the pelvis. Even when metastases are present, only persistent, mild, vague abdominal symptoms would cause patients to seek medical attention. Physicians should consider the diagnosis of ovarian cancer in all patients presenting with ovarian masses, especially in women in the perimenopausal or postmenopausal age group. In women of reproductive age, the majority of ovarian masses will be of functional origin and these will respond well to an expectant management protocol. A careful history should include the nature, progression, and duration of the presenting symptoms. Specific signs and symptoms suggestive of an underlying malignancy such as pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, and difficulty in eating/feeling full should be specifically sought, especially when these symptoms have been persistent (present for <1 year and occurred > 12 days per month). Any significant family history of neoplasia, such as breast, ovarian, endometrial, colorectal, and pancreatic carcinoma should be noted. Family or personal history of endometriosis may be of value in better defining the potential differential diagnosis.

When a woman presents with a unilateral adnexal mass of probable functional origin, it is appropriate to repeat the ultrasound following the next menses to ensure resolution. Cysts or masses that continue to enlarge, become increasingly symptomatic, or attain a more worrisome appearance on ultrasound would then justify further investigation and management.

If the patient has had previous gynaecologic surgery, it is appropriate to obtain previous operative notes and pathology reports. Previous cystectomy for dermoid cyst, for example, or extensive endometriosis, may help predict the nature of the present disease, although it is important to remember that malignancy can occur in the presence of previous benign disease.

When history and/or imaging findings suggest the possibility of an underlying malignancy, a comprehensive physical examination should be carried out that includes assessments of the supraclavicular and inguinal nodal areas, auscultation of the chest, breast examination, and abdominal examination to detect ascites or abnormal masses. A combined pelvic and rectal examination should be done in the presence of any pelvic mass to assess the contour and consistency of the pelvic mass as well as the presence of pelvic nodularities. The presence of any of these signs or symptoms is suggestive of an underlying malignancy. Serum CA125 level measurement should be considered prior to surgical intervention, especially in a situation where the risk of underlying malignancy is elevated. It is important to be aware of the range of normal CA125 in each specific laboratory used, as many different assays are currently in use with different upper limit of the normal range.

ULTRASOUND EXAMINATION

Transvaginal pelvic/transabdominal ultrasound is a readily available investigation that can provide information to assist physicians in assessing the malignant potential of an adnexal/ovarian mass. Because of the proximity of the ovaries to the transvaginal probe, detailed examination of the appearance and internal structure of the ovarian/adnexal mass can be performed. The size of the mass should be reported, whether it is unilateral or bilateral, and the origin (ovarian or extra ovarian) determined, if possible. A complex multilocular mass, thick septations, presence of papillary excrescences and solid components, increased central vascularity within the mass, and evidence of ascites and peritoneal nodularities have been shown to be predictive of an increased risk of malignancy.

RISK OF MALIGNANCY INDEX

A risk of malignancy index (RMI) has been proposed and validated to identify patients at high risk of ovarian cancer. Two scoring schemes exist, RMI I and RMI II, each of which derives scores using ultrasound features, menopausal status, and preoperative CA125 level (using assays with a normal CA125 being less than 35 U/mL) according to the following equation:

\[
\text{RMI score} = \text{ultrasound score} \times \text{menopausal score} \times \frac{\text{CA125 level in U/mL}}{35}
\]

The original RMI I scoring system and the revised RMI II system are both outlined in Table 2. Three studies have compared the two RMI scoring schemes, using cut-off RMI score above 200 to indicate high malignancy risk. The RMI II score was more sensitive than the RMI I system, with a specificity of 89% to 92% and positive predictive values around 80%. Because of its simplicity and reproducibility, the RMI II scoring system is recommended to provide an objective assessment of the underlying malignant potential, using a cut-off score of 200. To facilitate computation of the RMI II score, it is recommended that each ultrasound report done for assessment of an ovarian mass is standardized to include the required variables to compute the RMI score. In patients with an abnormal RMI score based on ultrasound findings and suggestive clinical signs and symptoms of malignancy, further radiographic evaluations such as CT/MRI prior to subspecialty referral are unlikely to be beneficial.
FUTURE DIRECTIONS

Active research is ongoing to develop better screening tests to detect early ovarian cancers and improve diagnostic accuracy of existing imaging modalities.\textsuperscript{18,19}

ROLE OF THE GYNAECOLOGIC ONCOLOGIST IN THE MANAGEMENT OF OVARIAN CANCER

Over the past few decades, there has been an increased emphasis on subspecialty training in the management of various cancers. For ovarian cancer, both centralized care\textsuperscript{20,21} and initial surgery by a gynaecologic oncologist resulted in improved outcomes.\textsuperscript{22,23} The management of ovarian cancer can be broken down into early (stage I/II) and advanced (stage III/IV) disease.

Early Stage Disease

The management of patients with clinically confined disease to the ovary centres on comprehensive surgical staging to rule out occult metastatic disease. Patients thought to have disease clinically confined to the ovaries are upstaged approximately 30% of the time when further comprehensive surgical staging is performed.\textsuperscript{24}

Comprehensive surgical staging should include the following:

1. Bilateral salpingo-oophorectomy and hysterectomy in postmenopausal women. A more limited surgery may be acceptable in young women wishing fertility preservation.
2. Infra-colic omentectomy
3. Peritoneal fluid sampling or pelvic washings
4. Biopsy of any suspicious peritoneal nodules/adhesions or random peritoneal biopsies from all intra-abdominal serosal surfaces
5. Bilateral diaphragmatic scraping/biopsies

6. Retroperitoneal lymph node evaluations to include both bilateral pelvic and para-aortic nodal areas

The contributions of the gynaecologic oncologist to the management of early ovarian cancer can be assessed in the following clinical situations:

1. Lower recurrence rates

In a retrospective review, Le et al.\textsuperscript{25} compared recurrence rate in patients who had minimal surgical staging and liberal use of adjuvant chemotherapy with a similar group of patients who had comprehensive staging with more stringent criteria used for adjuvant therapy based on surgical findings. The odds ratio for recurrence was 2.62 (95% CI, 1.09–6.32) in patients not comprehensively staged.

2. Improved overall survival

Studies looking at a relationship between surgeon and survival in early stage ovarian cancer show a trend towards improved survival when gynaecologic oncologists are performing the surgery.\textsuperscript{26} One study involving 47 patients by Mayer et al.\textsuperscript{27} found patients operated on by gynaecologic oncologists had a 24% improvement in five-year overall survival when compared with those patients operated on by general surgeons and general gynaecologists (\(P < 0.05\)).

When patients with clinically apparent early ovarian cancer are not staged, consideration is often given to repeat surgery to assist with the decision regarding needs for subsequent adjuvant treatment. The prospect of two surgeries increases the risk for surgical morbidity and increases cost to the health care system. Elit et al.\textsuperscript{28} reported the relative risk of re-operation to be significantly decreased when gynaecologic oncologists were present at time of initial surgery. The significance of comprehensive staging was demonstrated recently in the ACTION trial,\textsuperscript{29} conducted in Europe. Patients who are optimally staged according to strict protocol and who are proven to truly have surgically stage I disease have a low recurrence rate and high overall survival.

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**Table 2. The risk of malignancy index (RMI) scoring system**

<table>
<thead>
<tr>
<th>Ultrasound features</th>
<th>RMI I score</th>
<th>RMI II score</th>
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<tbody>
<tr>
<td>Multilocular cyst</td>
<td>0 = no abnormality</td>
<td>1 = no or one abnormality</td>
</tr>
<tr>
<td>Presence of solid areas</td>
<td>1 = one abnormality</td>
<td>4 = two or more abnormalities</td>
</tr>
<tr>
<td>Bilaterality of lesions</td>
<td>3 = two or more abnormalities</td>
<td></td>
</tr>
<tr>
<td>Presence of ascites</td>
<td>1 = no or one abnormality</td>
<td></td>
</tr>
<tr>
<td>Presence of intra-abdominal metastasis</td>
<td>1 = no or one abnormality</td>
<td></td>
</tr>
<tr>
<td>Prenopausal</td>
<td>3 = two or more abnormalities</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>U/mL</td>
<td>U/mL</td>
</tr>
</tbody>
</table>

Example: A postmenopausal woman with a multilocular cyst with solid areas with ascites and a CA125 level of 100 has a RMI II score of 4 \(\times 4 \times 100 = 1600\).
survival even without adjuvant chemotherapy. Patients who are sub-optimally staged are more likely to require adjuvant chemotherapy.  

Advanced Disease

The inverse relationship between residual tumour volume and survival in patients with ovarian cancer was first described by Griffiths in 1975, and several studies have shown an improved rate of optimal debulking and improved overall survival when patients with ovarian cancer whose initial surgery is performed by gynaecologic oncologists. An evidence-based review looking at the relationship between surgical speciality and survival in patients with ovarian cancer found a six- to nine-month median survival benefit in patients managed initially by gynaecologic oncologists.

Recommendations

The quality of evidence reported in this document has been assessed using the Evaluation of Evidence criteria in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

1. Primary care physicians and gynaecologists should always consider the possibility of an underlying ovarian cancer in patients in any age group presenting with an adnexal or ovarian mass. (II-2B)

2. Appropriate workup of a perimenopausal or post menopausal woman presenting with an adnexal mass should include evaluation of symptoms and signs suggestive of malignancy, such as persistent pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, and difficulty eating. In addition, CA125 measurement should be considered. (II-2B)

3. Transvaginal or transabdominal ultrasound examination is recommended as part of the initial workup of a complex adnexal/ovarian mass. (II-2B)

4. Ultrasound reports should be standardized to include size and unilateral/bilateral location of the adnexal mass and its possible origin, thickness of septations, presence of excrescences and internal solid components, vascular flow distribution pattern, and presence or absence of ascites. This information is essential for calculating the risk of malignancy index II score to identify pelvic masses with high malignant potential. (IIIC)

5. Patients deemed to have a high risk of an underlying malignancy should be reviewed in consultation with a gynaecologic oncologist for assessment and optimal surgical management. (II-2B)

REFERENCES


