Ovarian cancer – not quite a ‘silent killer’

Ovarian cancer is often asymptomatic until the late stages, but there are certain signs to look out for, write Peter Hayes and Siobhan Carruthers

OVARIAN CANCER IS A SERIOUS DISEASE. According to the Irish Cancer Society, there are 300 or so new diagnosed cases in Ireland per year and about 200 deaths. It often presents when a cure is no longer possible. There are few early warning signs; however, there are certain symptoms that GPs should be aware of. We want to highlight some of the few ‘warning shots’ that exist and follow on with a brief up-to-date review of many of the management issues.

Main risk factors

- Repeated ovulations (long menstrual lifetime, null parity, not breastfeeding, infertility)
- Genetics (BRCA gene/breast-ovary syndrome, Lynch syndrome/colon-ovary syndrome, strong family history of ovarian cancer)
- Postmenopausal oestrogen (hormone replacement treatment)
- Cigarettes and increased body mass index
- Endometriosis (2.5% lifetime risk of ovarian malignancy).

Symptom watch for ovarian cancer

- Abdominal/pelvic pain
- Abdominal swell/bloating
- Feeling unusually full post meals
- Urinary urgency.

If any of these symptoms are present in women, especially in those over 50 years, then the symptom index is positive. These symptoms, if present for less than one year and are present more than 12 times per month, give a sensitivity of 56% for early disease and 79.5% for late disease. The specificity is 86.7%-90%.

If you combine the symptom index being positive with either a raised CA-125 or the new ovarian tumour marker HE-4, then the sensitivity becomes 84% and the specificity 98%. A new onset of irritable bowel disease-type symptoms in a woman over 50 years should also ring an alarm bell about ovarian cancer issues. Colonoscopy referral, while important, should maybe occur parallel to gynaecological referral.

Signs

The signs of ovarian cancer are notoriously silent until the late stages of the disease when a patient will often have:

- Pelvic mass on exam and/or ascites/pelvic lymph nodes.
- Unexplained weight loss
- Fatigue
- Changes in bowel habit

Symptoms not suggestive of ovarian cancer

- Abdominal swell/bloating
- Feeling unusually full post meals
- Urinary urgency,

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**Table 1**

<table>
<thead>
<tr>
<th>Symptom Watch for Ovarian Cancer</th>
<th>Ovarian Cancer Suspected?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal/pelvic pain</td>
<td>Yes</td>
</tr>
<tr>
<td>Abdominal swell/bloating</td>
<td>No</td>
</tr>
<tr>
<td>Feeling unusually full post meals</td>
<td>Yes</td>
</tr>
<tr>
<td>Urinary urgency</td>
<td>No</td>
</tr>
<tr>
<td>Persistent abdominal distension</td>
<td>Yes</td>
</tr>
<tr>
<td>Feeling full (early satiety)</td>
<td>No</td>
</tr>
<tr>
<td>Pelvic or abdominal pain</td>
<td>Yes</td>
</tr>
<tr>
<td>Increased urinary urgency</td>
<td>No</td>
</tr>
<tr>
<td>Woman is 50 years or over and has had symptoms within the last 12 months that suggest IBS</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Detection of Ovarian Cancer in Primary Care**

1. **Woman presents to GP**
   - Physical examination identifies ascites and/or a pelvic or abdominal mass (not obviously uterine fibroids)
   - Woman reports having any of the following symptoms persistently or frequently – particularly more than 12 times per month especially if she is 50 years or over:
     - Persistent abdominal distension (‘bloating’)
     - Feeling full (early satiety)
     - Pelvic or abdominal pain
     - Increased urinary urgency and/or frequency
   - Woman is 50 years or over and has had symptoms within the last 12 months that suggest IBS
   - Measure serum CA125
     - ≥ 35 IU/ml
     - < 35 IU/ml
   - Arrange ultrasound of abdomen and pelvis
     - Normal
     - Suggestive of ovarian cancer
   - Refer urgently

2. **Ovarian cancer suspected?**
   - Yes
   - Assess carefully: are other clinical causes of symptoms apparent?
     - Yes
     - Investigate
     - Advise her to return if symptoms become more frequent and/or persistent
   - No

*Adapted from NICE 2011 [www.nice.org.uk/cg122](http://www.nice.org.uk/cg122)*
Diagnosis
All cases with suspicious symptoms or signs should be referred from primary to secondary care for assessment. This will involve examination and imaging with ultrasound if not already performed. A CA-125 tumour marker should also be performed.

Care pathway (adapted from NICE 2011)
If a patient presents with the following symptoms they may be managed initially in primary care according to the skill level of the practitioner:

- Positive symptom index (listed previously)
- New irritable bowel type symptoms aged over 50 years
- Anxiety about risk factors.

GP with little experience in gynaecology: Refer all of the above groups to secondary care for opinion.

GP with some training in gynaecology: Perform a CA-125 serum test and refer if higher than accepted limits. If the CA-125 is within normal limits, a careful re-evaluation of symptoms and re-assessment examination should take place. Further investigations to other organ systems can be organised if appropriate.

GP with specialist interest in gynaecology: If CA-125 is elevated you may wish to order an ultrasound of pelvis. If the ultrasound does not show any suspicious signs of malignancy then a careful follow-up and monitoring process may take place. This should occur along with a careful re-evaluation of symptoms and re-examination to rule out the involvement of other organ systems.

The patient with ‘clinical signs’ on exam such as ascites or pelvic lymph nodes should be referred to secondary care expediently in all cases.

Screening without symptoms in the general population
The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial of the National Cancer Institute (2011) has recently published its findings. It performed yearly CA-125 blood tests on women for six years and annual ultrasound tests for four years. The effect of screening on this group’s mortality was dubious. Screening was felt to be unbeneficial. It was felt that screening probably causes harm, with far too many false positive patients being identified and operated on.

The UKTOCS trial is ongoing and will have results in late 2014. This trial compares three screening possibilities: a combined CA125 and ultrasound (if CA-125 raised) arm; an annual ultrasound screening arm; and no screening arm; an annual ultrasound screening arm; and no screening arm. The results are eagerly awaited.

Many combined tumour marker groups have been used in studies of general population screening for ovarian cancer. These combine CA-125 with other tumour markers in an attempt to increase specificity and sensitivity in these blood markers diagnosing ovarian cancer. None are proven, but the latest ongoing studies are using a panel profile of circa 30 blood tumour markers.

Staging
Staging details are usually not of relevance to primary care providers but with patients who are diagnosed with ovarian cancer surviving longer than ever before, it is plausible that these types of patients may need a ‘chronic-care’ type model of care (see Table 2).

Follow up for successful treatment of stage 1 and stage 2
Follow up every three months for two years, then every six months for a further three years and annually thereafter.

Research/other treatment options
Neo-adjuvant chemotherapy is also used in some centres for late stage disease where the chemotherapy happens before the de-bulking surgery.

Radiotherapy is not an option for most patients as the problems with pelvic irradiation outweigh the benefits.

Intra-peritoneal chemotherapy is currently in trials. The port is a trans-abdominal opening and placed at laparotomy/laparoscopy.

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References
5. Gynecology by ten teachers, Campbell and Monga. Hodder Education 2006
15. SIGN guidelines. www.sign.ac.uk/pdf/sign75.pdf

FORUM Women’s Health

Table 1: Cancer Screening and Survival Rates

<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment</th>
<th>Outcome/five-year survival</th>
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<tbody>
<tr>
<td>Stage 1a/1b</td>
<td>Surgery removing the uterus, fallopian tubes and one or both ovaries. Conservative surgery spares the uterus and one ovary</td>
<td>90% survival</td>
</tr>
<tr>
<td>Stage 1c/2</td>
<td>Surgery as above but with adjuvant chemotherapy</td>
<td>50% relapse within five years</td>
</tr>
<tr>
<td>Stage 3/4</td>
<td>Pelvic de-bulking operations and adjuvant chemotherapy but with eventual palliation. Treatment is decided on a person-by-person basis</td>
<td>Five-year survival low, 75% of cancers diagnosed here</td>
</tr>
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