Ovarian cancer – current management and future directions

Sian E Taylor

John M Kirwan

Abstract

Ovarian cancer has the highest mortality of all the gynaecological malignancies. Epithelial ovarian cancer is the most common subtype. Approximately 5–10% occurs in women with an inherited predisposition. These patients may benefit from prophylactic surgery. Diagnosis involves measurement of CA 125 and ultrasound. The results of both are combined to give a risk of malignancy index; this is used to decide where treatment takes place. Treatment of advanced epithelial ovarian cancer usually involves debulking surgery and chemotherapy. The correct order of these treatments is currently being evaluated. There are survival benefits if surgery is performed by a specialist gynaecological oncologist. Current standard chemotherapy for epithelial ovarian cancer is carboplatin with paclitaxel. Treatment may prolong life and palliate symptoms but it is rarely curative. New treatments are constantly being developed and offer the hope of improved outcomes. These include radical surgery, intraperitoneal chemotherapy and novel drug treatments.

Keywords chemotherapy; ovarian cancer; screening; surgery

Introduction

The lifetime prevalence of ovarian cancer in the developed world is 1–2%. It is often described as a silent killer, however, early symptoms of abdominal bloating, urinary frequency, a sensation of fullness and pelvic/abdominal pain, are common. As these symptoms are non-specific they are often dismissed by both patients and healthcare professionals. When it is detected it is usually at an advanced stage with a poor prognosis. In England and Wales, ovarian cancer kills more women than all of the other gynaecological malignancies combined. Survival for ovarian cancer patients in the UK has increased over time; however, the average survival still lags behind the Nordic countries and the USA.

Childbearing, breastfeeding and use of the oral contraceptive pill all protect against the development of ovarian cancer. This is thought to be due to a reduced number of ovulatory cycles minimising the damage/repair cycle of the ovarian epithelium. It is likely that the increased incidence of ovarian cancer over the past few decades is partly due to reduced parity.

Patients with ovarian cancer are best managed by multidisciplinary teams. These usually include: nurse specialists, medical oncologists, histopathologists, radiologists, palliative care specialists and gynaecological oncologists in collaboration with the patients and their families.

Types of ovarian cancer

Primary ovarian tumour types include epithelial, sex cord-stromal and germ cell tumours. Tumours not specific to the ovaries also occur, such as sarcomas and lymphomas. Metastatic tumours from breast, stomach and endometrial primaries are not uncommon.

Epithelial tumours

More than 80% of ovarian cancer is epithelial in origin. Epithelial tumours classically arise from the cells covering the surface of the ovary, although some probably arise from the fimbrial end of the fallopian tube and others from endometriotic implants within the ovaries. The most common subtype is serous, accounting for about 50%, followed by endometrioid, mucinous, clear cell, transitional (Brenner), mixed and undifferentiated tumours.

Primary peritoneal can be clinically and histologically indistinguishable from metastatic epithelial ovarian cancer. It is diagnosed when a condition identical to disseminated peritoneal ovarian cancer arises in the absence of any clear ovarian primary. The treatment is the same as for ovarian cancer, although, as there is often no mass to debulk, chemotherapy is more often used as the primary treatment.

Borderline ovarian tumours also arise from the ovarian epithelium. They are not truly cancers but are termed ‘borderline’ because they show histological features that are intermediate between benign and malignant tumours. They occasionally spread beyond the ovary to produce implants in the omentum and the peritoneum. They can recur after long periods; cases have been documented with disease returning over 30 years after the initial presentation. They are typically found in a younger population than epithelial cancers, with one-third occurring in women under the age of 40 years. It is probable that they represent a form of premalignant disease for low grade ovarian carcinomas.

Sex cord-stromal tumours

Sex cord-stromal tumours account for approximately 7% of all malignant ovarian tumours. They arise from a combination of the hormone producing cells of the ovary and stromal fibroblasts. Around 70% of all malignant sex cord-stromal tumours are granulosa cell tumours. Most occur in women in their sixth decade, although a small proportion arises in young women and prepubertal girls. Granulosa cell tumours are frequently oestrogen secreting, although androgen secreting varieties do occur. High levels of oestrogen can lead to endometrial pathology, including endometrial hyperplasia and carcinoma. Common presenting symptoms include abdominal distension, acute abdominal pain and abnormal vaginal bleeding. Most present at an early stage and have an excellent prognosis. Treatment is principally surgical with platinum-based chemotherapy for advanced or...
recurrent disease. Surgical treatment is as for epithelial ovarian cancer although in young women with early disease fertility preservation is an option. Other stromal tumours are rare and include thecomas, fibromas, Sertoli-Leydig cell tumours and gynandroblastomas.

**Malignant germ cell tumours**

Malignant germ cell tumours occur chiefly in girls and young women. The most common variety is the dysgerminoma, the counterpart to the seminoma in the male. Other types include the yolk sack tumour, embryonal carcinoma, polyembryoma, non-gestational choriocarcinoma and teratoma. They usually present with abdominal pain, which is sometimes acute, and a palpable pelvic mass. Several of these tumours secrete tumour markers, which are useful in diagnosis and monitoring (e.g. alpha-fetoprotein, human chorionic gonadotrophin and lactic dehydrogenase). Treatment is primarily surgical. As over 60% are confined to one ovary at diagnosis, fertility sparing surgery is usual with unilateral salpingo-oophorectomy or even ovarian cystectomy in selected cases with otherwise normal ovaries. Dysgerminomas are unusual ovarian tumours in that they are highly radiosensitive. However, as this usually results in premature ovarian failure, platinum-based chemotherapy is currently the preferred option. Non-dysgerminoma tumours are treated with the chemotherapy combination of bleomycin, etoposide and cisplatin. Response rates are excellent with cure rates approaching 100% in early stage disease and up to 75% in advanced disease.

**Familial ovarian cancer**

Approximately 5–10% of all ovarian cancer is associated with a genetic predisposition. These cancer syndromes are inherited in an autosomal dominant fashion. Individuals carrying these gene defects have a significantly higher risk of developing ovarian cancer than the general population (Table 1).

A strong family history of breast and/or ovarian cancer, especially at a relatively young age, may indicate the presence of one of several possible BRCA 1 or BRCA 2 gene mutations. The products from these genes are involved in DNA repair and a damaged copy may be inherited from either parent. These gene mutations are often, although by no means exclusively, found amongst the Ashkenazi Jewish population. Men carrying these genes are at increased risk of pancreatic cancer as well as male breast cancer.

<table>
<thead>
<tr>
<th>Approximate lifetime percentage risk of developing ovarian cancer</th>
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<tr>
<td><strong>General population</strong></td>
</tr>
<tr>
<td>One 1st degree relative affected under 55 years</td>
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<tr>
<td>One 1st degree relative affected over 55 years</td>
</tr>
<tr>
<td>Two 1st degree relatives affected</td>
</tr>
<tr>
<td><strong>BRCA 1 carrier</strong></td>
</tr>
<tr>
<td><strong>BRCA 2 carrier</strong></td>
</tr>
<tr>
<td><strong>HNPCC carrier</strong></td>
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HNPCC, hereditary non-polyposis colorectal cancer.

Table 1

Endometrial, colon, ovarian and other cancers cluster in families with the Lynch 2 or hereditary non-polyposis colorectal cancer (HNPCC) syndrome. It is important to recognise that families with several different types of cancer may have a single underlying mutation. Careful family history and referral to the Cancer Genetics Team should follow locally agreed guidelines.

Prophylactic risk-reducing surgery is recommended for BRCA 1 and 2 carriers when they reach the age of 35 years and have completed their family. This usually consists of laparoscopic bilateral salpingo-oophorectomy. HNPCC carriers are also offered hysterectomy with bilateral salpingo-oophorectomy when their family is complete. Until patients are ready to undergo surgery, annual screening is offered with carbohydrate antigen 125 (CA 125) and transvaginal ultrasound. Neither prophylactic surgery nor screening can completely eliminate the possibility of developing cancer. Screening is unproven to improve survival and even if the ovaries are removed there is a small continuing risk of developing primary peritoneal cancer.

The lack of one of these specific cancer syndromes does not exclude an increased cancer risk as other rare syndromes also exist and not all inherited ovarian cancer syndromes have had their genetic origin fully characterised.

**Screening**

Screening with a combination of CA 125, ultrasound and pelvic examination is performed for patients with a family history of ovarian cancer. CA 125 is a glycoprotein that is released into the bloodstream by any condition that disturbs the peritoneum. Non-cancer conditions that induce this include cirrhosis of the liver, congestive cardiac failure, endometriosis and pelvic inflammatory disease. Pregnancy also causes a variable increase in serum levels. Epithelial ovarian cancer, particularly of the serous subtype, can cause dramatic increases in CA 125. This is only likely to occur when the disease has already spread beyond the ovary. Mucinous ovarian cancer produces a more modest, if any, elevation in CA 125.

Based on promising results in some early studies two large multicentre trials investigating ovarian cancer screening have been set up in the UK, another in the USA is scheduled to finish this year. Data from the initial screen in the prostate, lung, colon, ovary (PLCO) trial has shown low predictive values for both CA 125 and transvaginal ultrasound (TV US) with a high rate of surgery for benign conditions. The results of the annual screening are awaited. The UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) is a randomised trial of primary CA 125 versus primary TV US versus no screening in postmenopausal women who do not have a significant family history of ovarian cancer. It has now finished recruitment but the results will not be available until 2011. The UK Familial Ovarian Cancer Screening Study (UKFOCSS) is an observational study investigating ovarian cancer screening in women with a greater than 1 in 6 risk of developing the disease. Annual TV US are undertaken in addition to 4-monthly blood investigations, including CA 125. This study is still recruiting and is not expected to report before 2012. All of these screening trials are directed towards detecting epithelial ovarian cancer, although other pathologies are often discovered incidentally.

Other screening strategies have been investigated in small studies. These include combining CA 125 with a symptom index
and the use of a combination of novel blood biomarkers such as leptin, insulin-like growth factor and prolactin. Inhibin may be of use as a marker for mucinous and granulosa cell tumours. In the future, it is possible that metabolic ‘fingerprinting’ technologies such as spectroscopy and metabolomics will play a part.

Investigation

As stated in the introduction, the first symptoms of ovarian cancer usually emerge some time before diagnosis. These commonly include early satiety, changes in bowel habit, bloating, urinary frequency, pelvic and abdominal pain. Whilst individually these symptoms are so common as to be unremarkable, when they occur frequently and several occur together, investigation is mandatory. That said, however, most small ovarian cancers confined to one ovary are asymptomatic.

Unfortunately, most ovarian cancers are already at an advanced stage at diagnosis. Patients often complain of abdominal swelling and discomfort due to ascites ± a large abdomino-pelvic mass. Eating is often difficult and patients may notice weight loss, apart from the distended abdomen. It is not uncommon for patients to present with a swollen leg secondary to a deep vein thrombosis. The classical description of a Sister Joseph’s nodule representing an umbilical metastasis is rarely seen and can occur with many intra-abdominal malignancies.

If ovarian cancer is suspected, an abdominal and bimanual pelvic examination is helpful to determine the presence of ovarian masses. Ultrasound is the next step in investigation. If this is abnormal a CA 125 level should be checked. The ultrasound findings and CA 125 level together are used to calculate the risk of malignancy index (RMI) taking into account the patient’s menopausal status.

\[ \text{RMI} = U \times M \times \text{CA125} \]

- \( U \) = Ultrasound score (1 point for each of multilocular cyst, evidence of solid areas, ascites, bilateral lesions, evidence of metastatic disease. \( U = 0 \) for 0 points, \( U = 1 \) for 1 point, \( U = 3 \) for 2–5 points).
- \( M \) = Menopausal status (premenopausal = 1, postmenopausal = 3).
- CA 125 = Serum CA 125 level.

A score of 200 or greater gives a sensitivity of 85% and a specificity of 97% for ovarian cancer. Using this level as a cut off, patients are triaged to either surgery in a cancer centre under the care of a specialist multidisciplinary team, including subspecialist gynaecological oncologists, or to care under a general gynaecologist with an interest in gynaecological oncology in a cancer unit.

In advanced disease, further imaging, such as computed tomography of the abdomen and pelvis, is often carried out to assess extent of disease and whether surgery is likely to optimally debulk the tumour. A chest x-ray is essential to check for evidence of thoracic spread, as are blood tests to assess renal and liver function. Other tumour markers such as carcino-embryonic antigen and CA 19-9 or investigations such as a barium enema may also be necessary to exclude alternative tumours.

Staging

Staging is performed to guide treatment and to provide information on prognosis. Traditionally, this has been achieved by performing a staging laparotomy. Information can also be gleaned from radiological investigations and cytology of ascitic or peritoneal fluid. The current staging system was devised by the International Federation of Obstetrics and Gynaecology (FIGO; see Table 2).

Treatment

Treatment in ovarian cancer depends upon the stage at presentation and the histological subtype. Non-epithelial cancers are discussed earlier. In general, epithelial ovarian cancers are treated with a combination of debulking surgery and platinum-based chemotherapy. Except in very early disease, treatment is rarely curative but it can provide symptom relief and prolong life.

### FIGO staging of ovarian cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>Confined to ovaries</td>
</tr>
<tr>
<td>Ia</td>
<td>One ovary, no ascites present containing malignant cells, no tumour on external surface, capsule intact</td>
</tr>
<tr>
<td>Ib</td>
<td>Both ovaries, no ascites present containing malignant cells, no tumour on external surfaces, capsule intact</td>
</tr>
<tr>
<td>Ic</td>
<td>Tumour limited to one or both ovaries with any of the following; tumour on the surface on one or both ovaries, capsule ruptured, ascites present with malignant cells or positive peritoneal washings</td>
</tr>
<tr>
<td>II</td>
<td>Growth involving one or both ovaries with pelvic extension</td>
</tr>
<tr>
<td>IIa</td>
<td>Extension and/or metastases to uterus and/or fallopian tubes</td>
</tr>
<tr>
<td>IIb</td>
<td>Extension to other pelvic tissues</td>
</tr>
<tr>
<td>IIc</td>
<td>Tumour stage IIa or IIb but with tumour on surface of one or both ovaries, capsule ruptured, ascites present containing malignant cells or positive peritoneal washings</td>
</tr>
<tr>
<td>III</td>
<td>Tumour involving one or both ovaries with microscopically confirmed peritoneal implants outside the pelvis and/or regional lymph node metastasis</td>
</tr>
<tr>
<td>IIIa</td>
<td>Microscopic peritoneal metastasis beyond the pelvis</td>
</tr>
<tr>
<td>IIIb</td>
<td>Macroscopic peritoneal metastasis beyond the pelvis, 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>IIIc</td>
<td>Abdominal implants greater than 2 cm in diameter and/or regional lymph nodes metastasis</td>
</tr>
<tr>
<td>IV</td>
<td>Distant metastasis beyond the peritoneal cavity. Includes liver parenchymal metastasis and/or pleural effusion with positive cytology</td>
</tr>
</tbody>
</table>

FIGO, International Federation of Gynecology and Obstetrics.
The order in which surgery and chemotherapy are best performed is not known. Classically, a staging and debulking laparotomy is performed followed by six cycles of chemotherapy. Second look laparotomy, where a second surgical assessment/debulking procedure is performed after completion of chemotherapy, is not beneficial. However, interval debulking surgery, performed midway through chemotherapy, is gaining popularity in the UK. Using this method, tumours that would not have been able to be optimally debulked may become amenable to surgery. The CHEmotherapy OR Upfront Surgery (CHORUS) and European Organization for Research and Treatment of Cancer (EORTC) 55791 trials are addressing this question.

**Surgery**

This traditionally involves a midline laparotomy, sampling of ascitic fluid or peritoneal washings for cytology, full assessment by inspection/palpation of all peritoneal surfaces and biopsy of any suspicious areas, removal intact of any encapsulated masses or debulking of tumour, sampling of suspicious pelvic and paraaortic lymph nodes, omentectomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy.

The primary aim of surgery is to remove as much tumour as possible to promote optimum response to chemotherapy, in addition to providing tissue for histological examination. Current guidelines from the Gynaecologic Oncology Group (FIGO) suggest that optimal debulking is defined as individual residual tumour deposits measuring 1 cm or less in maximum diameter. The evidence for debulking improving chemosensitivity is not absolute. Many argue that the ability to perform optimal cytoreduction is more a reflection of favourable tumour biology with an intrinsically better prognosis than the surgery itself influencing outcome. However, it has been demonstrated that survival in grade III disease is improved by the primary surgery being performed by a specialist gynaecological oncologist, rather than an obstetrician/gynaecologist or a general surgeon.

Surgical aggressiveness varies considerably between continents, countries and individual units. Some studies have shown complete debulking rates of over 80% with ultra-radical surgery, including bowel resection, peritoneal stripping procedures and splenectomy. Published case series show small increases in mortality and morbidity. However, these studies usually involve highly selected cases from single institutions in the USA and may not be directly applicable to wider practice. Some disease remains unresectable even to the most adventurous surgeon; this includes small bowel mesenteric disease, disease of the portal aortic lymph nodes, omentectomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy.

Lymphadenectomy is also an area where practice differs, from the extreme of full dissection even with stage IV disease, to unilateral dissection only when stage Ia disease is suspected, to removal of only clinically involved nodes. The publication of a large randomised clinical trial with long follow-up, however, showed there was no overall survival advantage from routine systematic lymphadenectomy. Coupled with the excess toxicity of the procedure, many oncologists conclude that there is no role for systemic lymphadenectomy as part of initial ovarian cancer debulking.

There is also a trend towards less aggressive surgery in early epithelial ovarian cancer in young women who wish to preserve their fertility. About 8% of stage I epithelial ovarian cancers occur in women under the age of 35 years. A proportion of these will not have completed childbearing and may wish to consider fertility sparing surgery. Suitable patients include those with stage Ia, grade I or possibly grade II disease. Such conservative surgery would typically consist of peritoneal fluid cytology, unilateral salpingo-oophorectomy, omental biopsy, careful inspection of the contralateral ovary and possibly unilateral pelvic node dissection ± para-aortic node dissection. One case series describes 282 women treated conservatively for epithelial ovarian cancer. Just over 30% subsequently went on to have term deliveries. A total of 4% died of conditions related to their disease.

Surgery also plays a role in palliative care of patients with ovarian cancer. Bowel obstruction is common in the end stages of the disease, post-mortem studies of women dying with ovarian cancer revealed bowel obstruction in almost 50%. Before contemplating such surgery, consideration must be given as to whether it is appropriate. Surgery should only be performed if it has a reasonable chance of success and risks need to be carefully balanced against potential symptom relief. Contraindications to surgery include rapidly accumulating ascites, high obstruction, multiple levels of obstruction and poor performance status. Decisions involving palliative surgery should involve the multidisciplinary team and careful discussion with the patient and her relatives.

**Chemotherapy**

The current standard first-line chemotherapy regimen for ovarian cancer involves intravenous administration of a platinum-based drug combined with a taxane, usually paclitaxel, given 3 weekly for six cycles. Most centres have replaced cisplatin with carboplatin as it has a less toxic side-effect profile. Evidence for the use of paclitaxel is drawn from its efficacy in relapsed ovarian cancer. However, paclitaxel significantly increases the risk of toxicities such as neuropathy and hair loss when compared with carboplatin alone (for these reasons it is not universally used as a first-line treatment). Currently in the UK, around 25% of patients are treated with single agent carboplatin.

Impressive gains in progression-free and overall survival have been achieved in recent times with intraperitoneal (IP) chemotherapy but this comes at a price. The peritoneum is a large vascularised surface, promoting drug absorption and allowing prolonged high concentrations of drug to be in contact with the tumour site. Morbidity, especially IP catheter-related problems and pain, and treatment-related mortality are significantly worse with IP chemotherapy. The three large trials of IP chemotherapy did not use the current gold standard therapy of intravenous carboplatin and paclitaxel as a control. For these reasons, together with concerns about the optimal dosage regimen and organisa-

tional problems, IP chemotherapy has not been widely adopted, despite a National Cancer Institute announcement in 2006 recommending its implementation. However, selected patients with optimal tumour debulking and good performance status are likely to benefit from this treatment and it may, in time, gain acceptance. Current trials are investigating less toxic schedules, of comparing IP carboplatin and IP cisplatinum.

Epithelial ovarian cancer is one of the more chemosensitive solid tumours and complete clinical and radiological response occurs in up 50% with the above regimen, and about 15% are platinum resistant. Unfortunately, most patients with advanced ovarian cancer will relapse. Chemotherapy for recurrent disease
is determined, in part, by the length of time before relapse occurs. If relapse occurs more than 6 months afterwards, it is potentially platinum sensitive and, unless contraindicated, a regime containing platinum will be used again. Response rates are in the order of 30%. If relapse occurs within 6 months, second-line drugs, such as liposomal doxorubicin and topotecan or even experimental drugs may be considered as the outcome of this category is poor. As response rates are in the order of 10–20%, the choice of drug is made taking account of side-effect profiles and ease of administration.

Novel chemotherapeutic agents are constantly being developed. Current avenues being pursued in ovarian cancer include hormonal therapies, anti-angiogenic drugs and growth factor inhibitors. Hormonal therapies probably act by reducing oestrogen activity and include tamoxifen, aromatase inhibitors and gonadotrophin-releasing hormone analogues. Response rates of 10–15% have been achieved in relapsed disease. Their main advantage is their minimal side effects when compared with conventional chemotherapy. (Table 3)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side effects</th>
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<tbody>
<tr>
<td>Carboplatin</td>
<td>Fatigue, nausea and vomiting, myelosuppression, nephrotoxicity, subfertility, metallic taste, loss of taste, reduced appetite, peripheral neuropathy, allergic reactions</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Fatigue, nausea and vomiting, nephrotoxicity, ototoxicity, myelosuppression, subfertility, loss of appetite, peripheral neuropathy, metallic taste, loss of taste, allergic reactions, visual disturbance (blurred vision and altered colour vision)</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Fatigue, nausea and vomiting, myelosuppression, alopecia, peripheral neuropathy, myalgia, arthralgia, mouth ulcers, diarrhoea, rash, anaphylaxis, subfertility, headaches, abdominal pain, bradycardia</td>
</tr>
<tr>
<td>Liposomal doxorubicin</td>
<td>Fatigue, myelosuppression, nausea and vomiting, mouth ulcers, pain swelling or redness of palms and soles (palmar-plantar syndrome), diarrhoea, constipation, photosensitivity, alopecia, anaphylaxis, rash, cardiomyopathy</td>
</tr>
<tr>
<td>Topotecan</td>
<td>Fatigue, myelosuppression, nausea and vomiting, alopecia, diarrhoea, constipation, fever and flu-like symptoms, mouth ulcers, loss of appetite, dyspnoea, abdominal pain, rash, headache</td>
</tr>
<tr>
<td>Bevacizumab (currently unlicensed)</td>
<td>Hypertension, nausea, constipation, diarrhoea, fatigue, myalgia, arthralgia, delayed wound healing, nephrotic syndrome, thrombocytopenia, poor appetite, allergic reactions, neutropenia, thromboembolism, congestive cardiac failure, bowel perforation, reversible posterior leuкоencephalopathy syndrome, hypertensive encephalopathy</td>
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One of the most promising developments is the monoclonal antibody to vascular endothelial growth factor (VEGF), bevacizumab. Vascular endothelial growth factor is an important factor in neoangiogenesis and a poor prognostic feature in ovarian cancer. Bevacizumab is already in use for advanced bowel carcinoma and renal cell carcinoma. Early studies in ovarian cancer are promising although there are concerns about an increased risk of bowel perforation. A large phase III trial of bevacizumab with carboplatin and paclitaxel after surgical debulking (ICON 7) is currently underway.

### Palliative care

Palliation is an integral part of the care of patients with ovarian cancer. Maintaining a balance between optimism and pragmatism, together with knowing when the emphasis of care should tilt towards palliation are some of the most challenging aspects of caring for this group of patients.

Almost all patients with advanced ovarian cancer, whether in the terminal phase or not, will have distressing symptoms that require treatment. These symptoms may be due to the disease itself or secondary to their treatment. Common symptoms include nausea, pain, loss of appetite, constipation and abdominal distension. This is too small a space to describe all the possible treatment strategies involved but it is worth emphasising a few principles. It is important to take a history, examine the patient and review the drug chart and case notes. Then consider what investigations may be helpful and what drug or intervention will best treat the most likely cause of her symptoms. These patients are usually complex with multiple problems; however, a logical and systematic approach will help to identify the best treatment. Subcutaneous infusions delivered by syringe driver are useful as they permit a steady concentration of drug and oral medications may be poorly absorbed. Several hospices publish their guidelines for managing symptoms in palliative care on the internet, which can be very helpful.

Finally, the physical needs of a seriously ill patient are only one facet of their care. Social, spiritual and emotional needs should also be addressed. This aspect of care is easily overlooked but can make the difference between a peaceful and a difficult death.

### Further Reading


Practice points

- Ovarian cancer is best managed within a cancer centre by a multidisciplinary team
- The risk of malignancy index is a useful tool in determining the management of ovarian masses
- Treatment involves a combination of surgery and platinum-based chemotherapy
- Fertility sparing surgery is possible in women with early stage disease


