Invasive cancer of the cervix

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Abstract

Invasive cervical cancer remains the second commonest female malignancy worldwide. Early-stage disease may be asymptomatic. Advances in imaging techniques have improved selection of the appropriate treatment approach. Treatment options vary for each stage. An excisional cone is sufficient for treatment of micro-invasive disease (Ia1) provided the margins are clear. The management of stage Ia2 disease is more controversial. Surgery and radiation have similar survival rates for stage Ib—Ila disease, while the combination of both increases morbidity. Later stage tumours (Iib—IV) should be treated with chemoradiation as this is related to improved survival but also higher short- and medium-term toxicity in comparison to radiotherapy alone. Fertility-sparing surgical techniques such as radical trachelectomy may be appropriate in selected cases. Management of recurrent disease depends on the initial treatment, the individual characteristics and the presence of distant disease. Management of cervical cancer during pregnancy remains a challenge and appropriate counselling on individual patient basis is necessary. As the disease usually affects young women, psychological morbidity is significant and emotional support is essential.

Keywords cervical cancer; cervical screening; chemoradiation; CIN; FIGO staging; radical hysterectomy; trachelectomy

Introduction

Cervical cancer remains the second commonest female malignancy worldwide. Three-quarters of affected women live in developing countries that experience the major burden of disease. The disease primarily affects younger active women and therefore, the total years-of-life lost is proportionately higher than that for most other cancers with a later onset.

Countries with established screening programmes face different challenges; improving outcome for women with advanced disease, preserving fertility in younger women who increasingly bear the greatest burden of the disease, and incorporating advances in medical technology such as positron emission tomography (PET) and minimal access surgery are some of those challenges. The realization that persistent infection with oncogenic high-risk human papillomavirus (HPV) is causally associated with cervical cancer has been, undoubtedly, the most significant advance globally that led, more recently, to the development of prophylactic vaccines.

Epidemiology

Cervix cancer is the seventh in frequency cancer overall worldwide, with an estimated 493,000 new cases leading to 274,000 deaths in the year 2002 (Figure 1). The mortality is substantially lower than the incidence; worldwide, the ratio of mortality to incidence is 55%. Cervical cancer still remains an important public health issue in Europe with more than 66,000 new cases and 29,000 deaths annually. The majority of these cases are diagnosed in Eastern European countries (Figure 2). In the UK in 2006, there were 2873 registrations, and 941 deaths in 2007 (Figure 3).

Screening programmes have led to both reduced incidence and down staging of the disease with around a third of cancers being diagnosed as stage I. In the UK, it is estimated that screening saves approximately 5000 lives every year. The benefits are more obvious since the reorganization of the service in 1988 and the increase in coverage (from 35% in 1988 to 85% in 1998). The incidence of cervical cancer has fallen in the UK by 44% since 1975, and mortality from 7.1 per 100,000 in 1988 to 2.4 per 100,000 in 2007 (Figure 4).

The incidence rate for cervical cancer peaks at the age range 30–40 years of age, declines in incidence for older age groups but peaks again in the early 80 years age band (Figure 5).

Pathological subtypes

The majority of cervical cancers are squamous in origin, but adenocarcinomas appear to be increasingly common, accounting for approximately 20% of all primary cervical cancers. This increase partly reflects an increased awareness of the disease. Adenocarcinoma is more likely to be diagnosed in younger women and has largely poorer prognosis in comparison to cervical squamous carcinoma, which partly reflects the delay in diagnosis. Cytology screening programmes were designed to detect squamous lesions and, as a result, the endocervical distribution of glandular abnormalities reduces their accuracy. Specific oncogenic HPV types, and in particular HPV 18, have been related to adenocarcinoma.

The rare, but aggressive small-cell neuroendocrine-type squamous carcinoma typically behaves like similar disease arising from the bronchus. Adenocarcinomas can be pure but a significant proportion (40%) has mixed adeno-squamous cells, the adenosquamous carcinoma. Adenocarcinomas include many more histological subtypes than squamous cancers. About 80% are made up of cells of the endocervical type with mucin production.

Patterns of spread

Cervical cancers spread

- by direct spread into the cervical stroma, parametria and beyond, into the vagina, the body of the uterus, the bladder and the rectum.
- by lymphatics spread into parametrial, pelvic sidewall and para-aortic nodes. The incidence of pelvic lymph node and...
para-aortic disease according to stage is illustrated in Table 1.

- by blood-borne spread, although it is unusual

**Clinical management**

**Presentation**
The symptoms associated with cervical cancer are common, non-specific and usually associated with later stage disease. Early-stage disease may be asymptomatic and suspected on a cervical sample or diagnosed following treatment for cervical precancer, commonly in the form of large loop excision of the transformation zone (LLETZ). The classical signs and symptoms are irregular vaginal bleeding, especially post-coital and abnormal appearance of the cervix. Invasive cancer is rare in women with post-coital bleeding, but assessment is merited as it is much more common in this group than in the general population. Those symptoms are also common in women with *Chlamydia trachomatis* infection. Discharge and pain are often associated with more advanced disease.

**Diagnosis**
Diagnosis requires a biopsy for histopathological review by an experienced gynaecological pathologist. The biopsy needs to be large enough to demonstrate stromal invasion and often an appropriately sized loop diathermy (LLETZ) may be used. The optimal biopsy site is often the edge of the tumour that allows assessment of the transition from invasive to non-invasive. Central biopsies may reveal only pre-malignant or necrotic material, though often there may be no alternative. The tumours may bleed briskly after a biopsy and occasionally require packing. In very early disease, a cone with loop diathermy (LLETZ), knife (cold-knife conization) or diathermy needle (NETZ) can be diagnostic but also curative. Biopsies in a pregnant patient are important if invasion is suspected, but should be performed by an experienced clinician as significant bleeding may occur.

**Staging procedures**
Having established the diagnosis, the next step is to stage the disease, as this determines the ongoing management, it helps to assess prognosis and exchange of information among health professionals.

Cervix cancer is still staged clinically using the International Federation of Gynaecology and Obstetrics (FIGO) system (Table...
Traditionally, this included procedures such as pathology review, examination under anaesthesia with combined rectovaginal examination, cystoscopy, proctoscopy, chest radiography and perhaps intravenous urography. In practice, currently, all women undergo MRI, CT and possibly PET in some developed countries. Although the imaging results cannot change the clinical FIGO staging, they are often used to plan management. The MR imaging has high accuracy (90%) in describing the size, stage, extent of disease and permits detailed assessment of lymph nodes; it is obviously superior to CT and has commonly made the examination under anaesthetic combined with cystoscopy redundant. In this setting, PET-CT seems to enhance the accuracy in diagnosing involved lymph nodes and local invasion; more robust studies are required.

**Surgical staging:** several studies have described the use of sentinel nodes, which may be assessed by open or laparoscopic surgery. Some authors have reported 100% accuracy, but this technique is assessed only in the frame of research trials at present. In more advanced cancers, retroperitoneal or transperitoneal laparoscopic staging has been used to plan the field of radiation. Although several studies reported survival benefit following debulking of large nodes prior to radiation, the only available RCT showed surgical staging to be negatively correlated with outcome compared with non-interventional assessment. PET-CT seems to be an alternative accurate, non-invasive assessment tool to surgical staging.

**Management and treatment**
The principles of management are:
- tertiary review of pathology
- staging
- establishing the aim of treatment (i.e. curative or palliative)
- consideration of patient factors, age, fertility wishes, obesity, surgical and medical history, health status, preference
- treatment of local and possible metastatic disease
- presenting the patient with suitable options

Specialized multi-disciplinary gynaecological oncology teams should assess all the above factors and determine the optimum
management for each woman tailored to her individual characteristics. Decisions on how best to treat early disease in young women, especially when fertility-sparing techniques are considered, require considerable experience.

In principle, both surgery and radiotherapy are effective in early-stage disease (stage I and IIa), whereas locally advanced disease (stage IIb and above) relies on treatment by radiation or chemoradiation. A large RCT reported that radiation therapy and radical hysterectomy were equally effective in terms of 5-year overall and disease-free survival rates. Careful clinical staging by an experienced multidisciplinary team is clearly crucial in determining the appropriate treatment approach.

Surgery has obvious advantages; it permits conservation of ovarian function in premenopausal women, preservation of fertility in selected cases and also reduces the risk of chronic bladder, bowel and sexual dysfunction associated with radiotherapy. Surgery provides a histological sample and permits the assessment of risk factors, such as lymph node status, that influence prognosis. Complications in the hands of skilled surgeons are uncommon.

Stage Ia (Ia1 and Ia2)
In early cervical cancer, surgical excision alone can be curative. Correct staging and identification of early disease allows the selection of a group of women who are not at risk of lymph node disease and can be treated with less aggressive and, importantly, fertility-sparing therapy. There are two aspects to consider: adequate removal of local disease, and identification and treatment of distant disease.

In stage Ia1, the risk for lymph node involvement is virtually 0%. Consequently, complete excision of the invasive and pre-invasive disease with clear margins is commonly sufficient. The options of treatment include excision with knife or diathermy/laser or simple hysterectomy depending on woman’s wishes and fertility aspirations. The knife cone is often advantageous, in this setting, as the absence of thermal damage allows a more accurate assessment of the extent of invasion in comparison to a diathermy excision specimen. However, on many occasions, microinvasion is only diagnosed retrospectively as an incidental finding after loop excision for pre-invasive disease. Small adenocarcinomas can probably be treated in a similar manner. If disease is present at the margins, further excision or hysterectomy is recommended. If lymphovascular space invasion (LVSI) is present, the risk of nodal disease rises to 3.6%; although some clinicians advocate node dissection in this setting, the possible benefits must be balanced against morbidity and the risk of lymphoedema.

In stage Ia2, management of the disease is more controversial. The risk of pelvic lymph node involvement in this stage rises to...
Surgical options:

International Federation of Gynaecology and Obstetrics (FIGO) staging

**Stage I**

- **Stage Ia**: The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded)
  - Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm
  - Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm
  - Clinically visible lesion ≤4.0 cm in greatest dimension
  - Clinically visible lesion >4.0 cm in greatest dimension

- **Stage Ib**: Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina
  - Without parametrial invasion
  - With obvious parametrial invasion

**Stage II**

- **Stage IIa**: The tumour extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney
  - Tumour involves lower third of the vagina, with no extension to the pelvic wall
  - Extension onto the pelvic wall and/or hydronephrosis or non-functioning kidney

**Stage III**

- **Stage IIIa**: The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous oedema, as such, does not permit a case to be allotted to Stage IV
  - Spread of the growth to adjacent organs
  - Spread to distant organs

**Stage IV**

- **Stage IVa**: Spread of the growth to adjacent organs
- **Stage IVb**: Spread to distant organs

- **Stage Ia1**: Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≤5 mm and largest extension ≤7 mm
- **Stage Ia2**: Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm
- **Stage Ia3**: Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm
- **Stage Ib1**: Clinically visible lesion ≤4.0 cm in greatest dimension
- **Stage Ib2**: Clinically visible lesion >4.0 cm in greatest dimension

Table 2

<table>
<thead>
<tr>
<th>Stage Ib—IIa</th>
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<tr>
<td>Patients with stage Ib—IIa disease have two options: primary surgery or chemo-radiotherapy depending on the individual characteristics, co-morbidities and preferences.</td>
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</table>

**Surgical options:**

- **Radical hysterectomy and pelvic lymphadenectomy** — ensures complete excision of the tumour with adequate margins. There should be at least 5 mm clear margin from the tumour. The pelvic lymph node dissection should include obturator, internal, external and common iliac nodes. Para-aortic lymphadenectomy is not mandatory.

Complications in the hands of skilled surgeons are uncommon and include haemorrhage and direct trauma to the bowel, bladder, ureter or obturator nerve. Chronic bowel and bladder problems that require medical or surgical interventions occur in up to 8–13% of women due to parasympathetic denervation secondary to surgical clamping at the lateral excision margins. Prolonged bladder dysfunction requiring long-term intermittent self-catheterization is reported in 2.6% of patients overall and can be very distressing. Lymphoedema as a late complication that usually develops the first year after surgery, occurs in up to 8% of patients and is permanent. Although it is most commonly relatively mild, symptoms can be quite severe and significantly affect quality of life in 3% of the patients. Lymphocysts can also occur. Sexual function and psychological issues such as grieving over loss of fertility, altered body image, reduced vaginal size etc are not uncommon. The risk of fistula is about 1%.

Surgical approach has now been moving towards less aggressive, nerve-sparing techniques. The evidence reveals that more radical approaches offer no survival benefit and often lead to higher incidence of perioperative morbidity and chronic complications. Approximately 5%. A very conservative approach cannot be adopted; the pelvic lymph nodes must be surgically removed and assessed, while the management of the primary tumour remains less clear. When fertility preservation is an issue, radical trachelectomy and pelvic node dissection by a vaginal, laparoscopic or abdominal approach may be considered. Laparoscopic pelvic lymphadenectomy followed by a deep cold-knife conization has also been proposed; high quality evidence is still lacking. If fertility is not an issue, radical hysterectomy, or possibly simple hysterectomy and pelvic lymphadenectomy, should be recommended.

Stage Ib—IIa

Patients with stage Ib—IIa disease have two options: primary surgery or chemo-radiotherapy depending on the individual characteristics, co-morbidities and preferences.
bladder and bowel dysfunction. The Piver–Rutledge classification for radical hysterectomy is widely used (Table 3); newer classifications have also been proposed (Querleu–Morrow) (Table 4).

**Radical trachelectomy** — in other sites such as the breast and the vulva, the surgical treatment of cancer has become less radical and consists of wide local excision and regional lymphadenectomy/sentinel lymph node dissection without an adverse effect on cure rates. Gynaecological oncologists have attempted to apply the same principle for stage Ia2 and small volume stage Ib cervical tumours by adopting more conservative fertility-sparing techniques. Advanced maternal age and detection of early-stage disease as a result of screening increasingly enhance the value of these techniques.

Radical trachelectomy was first described by D’Argent in the mid-1980s and involves a radical excision of the cervix combined with either laparoscopic or open lymphadenectomy. The commonest route of trachelectomy is the vaginal approach, though more recently some surgeons are favouring an abdominal or laparoscopic approach that facilitates a greater excision of the parametrium. The insertion of abdominal or vaginal suture at the level of the isthmus that can accommodate a 6 mm Haeger dilator is recommended in attempt to prevent cervical incompetence. Intra-operative complications are rare. Post-operatively, about one-quarter of women suffer from dysmenorrhoea or, less commonly, from cervical stenosis, suture-related problems and dyspareunia.

Meta-analyses and large UK case series based on the vaginal approach have demonstrated recurrence rates of around 4%, with mortality of 2.3%. Most recurrences have occurred in high-risk pathological types, tumours over 2 cm in size and patients with LVSI. Of those attempting pregnancy, 70% delivered at term; the risk of premature delivery, late miscarriages and low-birth weight was substantially increased.

Careful selection of patients is crucial as detailed assessment may optimize outcomes and minimize adverse events. These decisions necessitate involvement of a multi-disciplinary specialized team with considerable experience.

### Piver–Rutledge classification of hysterectomy for cervical cancer

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>Extrafascial hysterectomy; removal of all cervical tissue</td>
</tr>
<tr>
<td>2</td>
<td>Modified radical hysterectomy; removal of medial 50% of the cardinal and uterosacral ligaments; uterine vessels are divided medial to the ureter</td>
</tr>
<tr>
<td>3</td>
<td>Equivalent to the classical Wertheim–Meigs operation; wide radical resection of the parametrium and paravaginal tissues; ureter dissected completely to bladder entry; uterosacral ligaments divided at origin; cardinals divided at pelvic sidewall</td>
</tr>
<tr>
<td>4</td>
<td>Ureter divided from pubovesical ligament; superior vesical artery ligated and upper 2/3 vagina excised</td>
</tr>
<tr>
<td>5</td>
<td>More radical procedure with possible bowel, bladder or ureteric dissection</td>
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Table 3

### Querleu and Morrow, classification of radical hysterectomy (2008)

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Type A</td>
<td>Minimum resection of paracervix</td>
</tr>
<tr>
<td></td>
<td>• This is an extrafascial hysterectomy. The paracervix is transacted medial to the ureter but lateral to the cervix. The uterosacral and vesicoureteric ligaments are not transacted at a distance from the uterus. Vaginal resection is generally at a minimum, routinely less than 10 mm, without removal of the vaginal part of the paracervix (paracolpos)</td>
</tr>
<tr>
<td>Type B</td>
<td>Transection of the paracervix at the ureter</td>
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<tr>
<td></td>
<td>• Partial resection of the uterosacral and vesicoureteric ligaments, ureter is unroofed and rolled laterally, permitting transsection of the paracervix at the level of the ureteral tunnel. At least 10 mm of the vagina from the cervix or tumour is resected</td>
</tr>
<tr>
<td>Type C</td>
<td>Transection of paracervix at junction with internal iliac vasculature system</td>
</tr>
<tr>
<td></td>
<td>• Transection of the uterosacral ligament at the rectum and vesicoureteric ligament at the bladder. The ureter is mobilized completely. 15–20 mm of vagina from the tumour or cervix and the corresponding paracolpos is resected routinely, depending on vaginal and paracervical extent</td>
</tr>
<tr>
<td>Type D</td>
<td>Laterally extended resection</td>
</tr>
<tr>
<td></td>
<td>• Rare operations feature additional ultra-radical procedures. The most radical corresponds to the laterally extended endopelvic resection (LEER) procedure</td>
</tr>
</tbody>
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### Lymph node dissection

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>External and internal iliac</td>
</tr>
<tr>
<td>2</td>
<td>Common iliac (including presacral)</td>
</tr>
<tr>
<td>3</td>
<td>Aortic infra-mesenteric</td>
</tr>
<tr>
<td>4</td>
<td>Aortic infra renal</td>
</tr>
</tbody>
</table>

This classification can be applied to fertility-sparing surgery and can be adapted to open, vaginal, laparoscopic or robotic surgery.

A large multicentric RCT initiated in Canada (SHAPE) is expected to clarify the optimal management of women with small volume disease.

**Stage Ib2** — management of bulky Ib tumours (specially stage Ib2) is controversial as these tumours are characterized by high rates of positive nodes and close surgical margins. Most centres offer chemo-radiotherapy as opposed to surgery but a few elect to operate; these centres have published equivalent survival data.
Prognostic factors — after surgery, histological examination of the specimen provides information on several prognostic factors that affect survival and are mentioned later. If the histology review suggests high-risk of recurrence with positive pelvic nodes and ‘close’ resection margins (≤0.5 cm), women are commonly offered adjuvant chemoradiation. Many institutions use the GOG score, which assesses factors such as size of tumour, the depth of invasion and LVI and gives the combination score that facilitates clinicians’ decision making.

Stage IIb–IV
Surgery with curative intent is not possible in women with advanced stages of disease. The available treatment modalities that offer potential of cure are radical radiotherapy and chemoradiation. Stage IVb is treated palliatively, often with a combination of chemotherapy and targeted radiotherapy.

Radical radiotherapy — aims to treat the primary tumour and metastatic pelvic lymph nodes. It is delivered by external-beam (teletherapy) that intends to treat any pelvic spread and intra-cavitary treatment (brachytherapy) that targets the primary site. The challenge of radiotherapy optimal dose planning is the ability to cure the primary disease and pelvic spread with the least possible morbidity to bowel, bladder and sexual function. The external-beam radiotherapy sessions to the pelvis are delivered daily usually over 20–30 days and are followed by brachytherapy, delivered locally to the cervix by High Dose Radiotherapy technique (HDR). Extended radiotherapy involving the para-aortic nodes increases morbidity with no significant survival benefit. It may be, however, appropriate in selected cases if para-aortic node involvement is indicated by PET scan and surgical staging.

Chemoradiation — there is now consensus that the use of concurrent cisplatin-based chemotherapy with radiotherapy is superior to radiation alone for the treatment of cervical cancer.

Follow-up
The evidence on the role of post-treatment surveillance in the detection of recurrent disease is inconsistent. Follow-up enables much more than detection of recurrent disease. It permits assessment of the complications of treatment, psychological, physical and psychosexual morbidity and provides reassurance. There is no role for cervical or vaginal vault cytology in the follow-up period except from women that had fertility-sparing procedures.

In cases of suspected recurrence, an MRI provides the most sensitive imaging modality that allows careful assessment of the disease distribution and is required before considering further treatment. In confirmed cases, a CT PET is commonly required for the assessment of distant metastasis/es and improved patient selection before planning radical treatment for apparently localized disease. The evidence demonstrates that this improves survival in operable cases and eliminates morbidity related to unnecessary interventions in unsuitable patients. Before considering further treatment, histological diagnosis is required followed by full re-staging.

Management of recurrent disease
The principles of the management of recurrent disease are similar to those of the primary tumour (see above). The exact treatment depends on the primary treatment, the site and stage of the recurrence, its resectability, treatment related morbidity and the effect on quality of life, the patient’s general health and wishes.

Women treated initially with surgery should be considered for radiotherapy. If the disease is apparently confined to the pelvis, radical chemo-radiotherapy is curative in 40–50% of cases. For those who have already undergone radiotherapy, the only potentially curative option is pelvic exenteration, provided the recurrence is central with no distant recurrence. Careful selection of cases and appropriate counselling is essential. In the hands of skilled surgeons and appropriate pre-operative assessment, this surgery can result in 5-year survival of 50%. Up to one-third of procedures are abandoned intra-operatively; PET-CT appears to help patient selection.

Palliation
In progressive advanced cervical disease, urinary tract symptoms, fistulae and distressing pain due to infiltration of the lumbosacral nerve plexuses are some of the common presentations. Ureretic obstruction and impaired renal function usually herald the terminal stage. Faeces and urine diversion with nephrostomies and stenting are only justified in cases where there is a curative intent. Chemotherapy with cisplatin is also palliative and should be restricted to primary late stage or recurrent cases that are not considered curable with other treatment options. It may increase life expectancy by a few months, but this must be balanced against quality of life. Pain control, psychological and emotional support is of paramount importance in the terminal phase.

Cervical cancer in pregnancy
Cancer of the cervix affects 1 in 10,000 pregnancies and represents about 1 in every 34 cases of cervical cancer. Two-thirds of women diagnosed in the first or second trimester have a stage Ib tumour. Diagnosis may be delayed, as the symptoms may be attributed to the pregnancy and colposcopic assessment of the
The pregnant cervix is not always easy; advice should be obtained from an experienced colposcopist. If invasion is suspected, an adequate biopsy in the form of loop, knife or wedge cone should be taken. The principles of management remain the same and treatment is similar stage for stage.

The disease can be safely staged at examination under anaesthesia, with a chest radiograph and by MRI. For stage Ia1 disease, despite a high rate of positive margins, an LLETZ or knife cone is usually sufficient. Traditionally, more advanced stages presenting before 20 weeks are treated immediately, those presenting after 28 weeks are treated post-delivery, while those presenting between 20 and 28 weeks of gestation remain in a grey zone. For stage I disease, diagnosed after 20 weeks, delaying treatment after delivery is often the most favourable option. Delivery around 32–34 weeks is justified after administration of steroids to promote fetal lung maturation. Caesarean radical hysterectomy is recommended after delivery of the fetus by classical incision. Chemoradiation will cause spontaneous miscarriage or fetal death.

The management of cervical malignancy in pregnancy remains a challenge to the patient, the family and the multi-disciplinary team involved. Careful sensitive counselling is essential. Decisions on continuing or terminating the pregnancy and the modality of treatment should be made in an individual basis.

Prognostic factors
There are several prognostic factors that influence survival:
- The stage of the disease
- The size, the volume and the depth of invasion
- The grade of the tumour
- The histological type, as small cell tumours have clearly been shown to be associated with a worse prognosis
- Lymphatic spread is probably the most important. The presence of positive nodes significantly reduces overall survival and LVSI is an additional prognostic factor
- Parametrial invasion
- Vascular invasion
- Status of resection margins in cases where surgery was performed

Survival
One- and five-year overall survival in patients with cervical cancer is shown in Figure 6.

Psychological impact
Cervical tumours commonly affect younger women and the effect of loss of fertility and early menopause is often significant. Treatment has a huge impact on the women’s psychological and sexual well-being; up to 50% of women have dyspareunia due to vaginal stenosis after chemo-radiation. These issues often need to be addressed by clinicians and in some cases referral to a counsellor might be necessary.

The future
The single greatest advance in the prevention of cervical cancer during the last decade has been the development of the prophylactic vaccine against two oncogenic HPV subtypes 16/18; it is estimated that this could reduce the incidence of cervical cancer by 70% in a high coverage population.

The use of MRI has improved the accuracy of the staging of cervical cancer. New imaging techniques such as PET-CT appear to improve the assessment of metastatic disease; this seems to be of value in the selection of the radiation field, particularly with regards to para-aortic nodes inclusion. PET appears also to be helpful in recurrent cases as the detection of disseminated disease influences management.

Research on the optimal management of early-stage disease in women who wish to preserve their reproductive potential is ongoing. More conservative surgical approaches that can reduce morbidity might prove to be equally efficient. Efforts to improve...
outcome for women with advanced disease, use of sentinel nodes and incorporation of medical technology advances such as PET and minimal access surgery are some of the challenges of the future.

FURTHER READING

Practice points

• Cervical cancer second commonest malignancy worldwide. Seventy-five percent of the cases are diagnosed in countries of the developing world that reflects the absence of screening.
• The implementation of an organized screening programme in the UK led to a significant decrease in the incidence of and mortality from cervical cancer.
• Persistent infection by oncogenic HPV types causes cervical cancer.
• Adenocarcinomas appear to be increasingly common, accounting for approximately 20—30% of all primary cervical cancers and have poorer prognosis.
• Micro-invasive disease can be treated by excisional cone alone.
• Surgery and chemoradiation for stage Ib/Ila disease have similar survival rates. Surgery has many advantages. Careful staging is important and allows selection of the most appropriate treatment modality as combination of both substantially increases morbidity without survival benefit.
• Advances in imaging with MRI and CT PET have improved management.
• Preservation of fertility is an option with fertility-sparing surgical techniques. Careful patient selection is required.
• The combination of chemotherapy and radiation significantly improves survival in comparison to radiotherapy but also short- and medium-term toxicity.
• Management in pregnancy remains a challenge and decisions should be individualized.
• The disease and its treatment can have a huge physical and psychological impact on women.