GUIDELINES

Management of cervical cancer: summary of SIGN guidelines

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Why read this?

Despite a well organised cervical screening programme for preinvasive disease in the United Kingdom, there are still about 2800 new cases of and 1000 deaths from cervical cancer each year.¹ Many patients still present to their general practitioner with symptoms associated with cervical cancer. The Joint Committee for Vaccination and Immunisation has announced the introduction of human papillomavirus vaccination for 12-13 year old girls next year, but it is predicted that it may take 40 to 60 years for an effect on the rates of cervical cancer to be seen.

This article summarises the most recent guidance from the Scottish Intercollegiate Guidelines Network (SIGN) on the management of cervical cancer.² The guideline aims to ensure that equitable standards of care are available to all women who develop cervical cancer and that the social and economic burden it places on women and their carers is minimised.

Recommendations

SIGN recommendations are based on systematic reviews of best available evidence, and the strength of the evidence is indicated as A, B, C, or D (fig 1). Recommended best practice ("good practice points") based on the clinical experience of the guideline development group is also indicated (as GPP).

Presentation

Intermenstrual bleeding, post-coital bleeding, and post-menopausal bleeding are common and non-specific symptoms and may be associated with cervical cancer or with other conditions such as genital *Chlamydia trachomatis* infection. The probability that a woman aged 45-54 developing post-coital bleeding in the community has cervical cancer is 1 in 2400 (which decreases with younger age to 1 in 44 000 for women aged 20-24).

- Test women with these symptoms for *Chlamydia* and treat if appropriate (D).
- If malignancy is suspected on examination (for example, a visible ulcerating or fungating lesion), women should be referred urgently for further investigation (GPP).
- Investigate post-coital bleeding as recommended in figure 2 (D, GPP).

- Unscheduled smears are not recommended outwith the screening programme (GPP).

After diagnosis of invasive cervical cancer

- Refer all women to a multidisciplinary team for optimal management (GPP). Women with cancer often have complex needs that cannot be tackled by a single specialty or discipline.
- Multidisciplinary team working should ensure a consistent and equitable approach to planning and managing care (GPP).
- Include specialist radiological review in multidisciplinary team assessment (GPP). This is essential for determining the most appropriate management, both at primary presentation and with relapsed disease or complications of treatment.
- For women with visible cervical carcinoma confirmed with biopsy—except women whose disease is classified by the International Federation of Gynecology and Obstetrics (FIGO) as stage IV (that is, when the tumour invades the mucosa of the bladder or rectum and/or extends beyond the true pelvis, or distant metastasis is present)—perform magnetic resonance imaging (B). (The table in the version on bmj.com outlines the FIGO staging criteria for cancer of the cervix and uterus.) Consider computed tomography for those with FIGO stage IV disease and those not suitable for magnetic resonance imaging (for example, owing to claustrophobia or the presence of metal implants) (B). In women not suitable for surgery because of the extent of their disease, consider positron emission tomography to identify unsuspected para-aortic lymph node metastases, which may modify their treatment (C). Computed tomography and magnetic resonance imaging are as accurate as intravenous urography in determining ureteric obstruction and give additional information, thus superseding the role of urography as a standalone investigation (C).
- Assess sexual function and concerns before treatment (GPP), and offer women information (B), training, (GPP) and support (C) for these before and after treatment. Problems experienced with cervical cancer may include loss of libido, change in sexual activity, and decreased intensity of orgasm.

This is one of a series of BMJ summaries of new guidelines, which are based on the best available evidence; they will highlight important recommendations for clinical practice, especially where uncertainty or controversy exists. See also Petignat P, Roy M. Diagnosis and management of cervical cancer. *BMJ* 2007;335:765-8. Further information about the guidance, a list of members of the guideline development group, and references w1-w8 are in the version on bmj.com.

The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation

- A**
- At least one high quality meta-analysis, systematic review of randomised controlled trials, or randomised controlled trial with a very low risk of bias and directly applicable to the target population; or
 - A body of evidence consisting principally of well conducted meta-analyses, systematic reviews of randomised controlled trials, or randomised controlled trials with a low risk of bias directly applicable to the target population, and demonstrating overall consistency of results
- B**
- A body of evidence including studies rated as high quality systematic reviews of case-control or cohort studies, and high quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population, and with overall consistency of results; or
 - Extrapolated evidence from studies described in A
- C**
- A body of evidence including well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population and with overall consistency of results; or
 - Extrapolated evidence from studies described in B
- D**
- Non-analytic studies, such as case reports, case series, expert opinion; or
 - Extrapolated evidence from studies described in C

Good Practice Points (GPP)

- ☒ Recommended best practice based on the clinical experience of the guideline development group

Fig 1 Explanation of SIGN grades of recommendations

- Offer surgical options, where appropriate, to women with operable disease who wish to preserve their fertility; such surgery would include radical trachelectomy (vaginal resection of the cervix and the upper 1-2 cm of the vaginal cuff), cold knife conisation (removal of a cone shaped sample of tissue from the cervix), or large loop excision of the transformation zone (C, D).

Fig 2 Investigation of post-coital bleeding

- Offer concurrent chemoradiotherapy with a platinum based chemotherapy to women whose disease is classed as one of the FIGO stages IB2 to IVA (that is, a clinically visible lesion over 4 cm to advanced disease without distant metastasis) (see the table on bmj.com) (A), with brachytherapy as an essential component (D). Surgery is not offered to this group of women because of the significant risk of positive margins and positive nodes. While women are having chemotherapy, monitor their haemoglobin concentrations and correct these as necessary (C).
- Offer hormone replacement therapy to women who have lost ovarian function (C).
- No evidence exists that pregnancy accelerates cervical cancer. Treatment may be delayed in early stage disease (FIGO stage IA or IB—that is, a lesion diagnosed only by microscopy; or a clinically visible lesion confined to the cervix) to allow fetal maturity (C). Fetal maturity and mode and timing of delivery should be assessed in consultation with an obstetrician (GPP). Make treatment decisions as for non-pregnant patients (C).

Follow-up

- Offer follow-up every four months for at least two years after treatment (GPP). Although three case series show that routine follow-up does not have a high sensitivity for detecting recurrent disease,⁵⁻⁷ it may have other benefits, such as detection of treatment complications and psychosexual and psychosocial morbidity.
- If lymphoedema develops (a possible complication of treatment or disease), offer access to a designated lymphoedema practitioner for information, support, and treatment (D and GPP).
- Consider magnetic resonance imaging or computed tomography (CT) initially to assess potential clinical recurrence in symptomatic women (C).

Management of recurrence or advanced disease

- If salvage therapy (either pelvic exenteration or radiotherapy) is being considered, perform whole body positron emission tomography (PET) or a PET-CT scan (B).
- Reserve pelvic exenteration for women with recurrent cervical cancer in the central pelvis in whom chemoradiotherapy has failed (D). To minimise mortality and morbidity, a dedicated multi-professional team should carry out total pelvic exenteration (GPP).
- Offer palliative chemotherapy to women whose disease is FIGO stage IVB (distant metastasis) or who have recurrent cervical carcinoma, after discussion of the relative benefits and risks (B).
- If a woman has advanced disease and her condition declines, offer comprehensive palliative care, as symptoms may be challenging and women may benefit from a wide variety of clinical services. Distressing problems associated with advanced cervical cancer include pain, renal failure from

National organisations supplying information and support for women with cervical cancer

- Jo's Trust (www.jotrust.co.uk)—Weedon Villa, Everdon NN11 3BQ; pamela@jotrust.co.uk
- Cancer Research UK (www.cancerresearchuk.org)—PO Box 123, Lincoln's Inn Fields, London WC2A 3PX
- Macmillan Cancer Support (www.macmillan.org.uk)—89 Albert Embankment, London SE1 7UQ; cancerline@macmillan.org.uk
- Lymphoedema Support Network (www.lymphoedema.org/lsn)—St Luke's Crypt, London SW3 6NH; adminlsn@lymphoedema.freemove.co.uk
- Maggie's Centres (www.maggiescentres.org)

bilateral ureteric obstruction, thrombosis, haemorrhage, malodorous discharge, and fistulas (C, D, GPP). Management of such problems should take account of the woman's personal views and circumstances—in particular, physical state, prognosis, and options for future therapy (GPP).

Psychosocial care and support

- Offer women tailored information and psychological support at diagnosis and throughout management (D, GPP) as cervical cancer has a considerable psychosocial impact on women and evidence exists that psychological and practical support may have a positive effect on their wellbeing.⁸ Carers, families, and dependants should be told about support available, including local and national organisations (the box) (D).
- Be aware of risk factors for psychosocial problems (see box 2 in the version on bmj.com).⁹ Individual risk factors include being young or having children under 21 years old; having economic or social difficulties; living alone; or having a history of psychiatric problems or substance misuse. Factors related to disease and treatment include having a poorer prognosis, more treatment side effects, greater functional impairment, lymphoedema, or chronic pain. If

KEY POINTS

Upper airway surgery for obstructive sleep apnoea in adults is resource intensive with low and inconsistent clinical effectiveness

Continuous positive airway pressure (CPAP) plus conservative weight and alcohol management should be first line treatment

When CPAP treatment fails, mandibular advancement devices may be considered (with conservative management) as second line treatment

Surgery for obstructive sleep apnoea should be done within controlled clinical trials; patients should be informed about the trial, as well as of the inconsistent results of surgery, its potential side effects, and the potential for relapse

there are concerns about the patient's psychological wellbeing, contact psychiatric or clinical psychology services (GPP).

Overcoming barriers

For pathologists, radiologists, and surgeons in particular, it is critical to establish what constitutes an adequate volume of cases for maintaining specialist skills. In the UK it is now accepted that only gynaecologists who have been appropriately trained should undertake radical hysterectomy and pelvic lymph node dissection.

The decline in the incidence of cervical cancer, as a result of well organised screening programmes, will lead to recognised gynaecological oncological surgeons in some regions of the UK having a very small number of cases.¹⁰ The acceptability of this situation is questionable, and the need for supraregional surgical centres must be recognised. Such centres will ensure that women get the best outcome from their surgery in terms of cure, lowest risk of side effects, and the possibility of appropriate, newer, less radical procedures, particularly where conservation of fertility is important. Concentrating surgery for cervical cancer in supraregional centres also enables adequately powered clinical trials to be designed and, importantly, completed in reasonable time.

In the UK, PET-CT scanning and contrast enhanced magnetic resonance imaging of the lymph nodes is becoming available for women with cervical cancer. The challenge for those charged with organising cancer services must be to ensure that appropriate imaging and surgery are available to all, not only to those who are treated at the cancer centres with the largest workload.

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- 1 Cancer Research UK. UK Cervical Cancer incidence statistics. Available from <http://info.cancerresearchuk.org/cancerstats/types/cervix/incidence/>
- 2 Scottish Intercollegiate Guidelines Network (SIGN). *Management of cervical cancer*. Edinburgh: SIGN, 2007.
- 3 Scottish Intercollegiate Guidelines Network (SIGN). *Management of genital Chlamydia trachomatis*. Edinburgh: SIGN, 2000.
- 4 Scottish Intercollegiate Guidelines Network (SIGN). *Investigation of post-menopausal bleeding*. Edinburgh: SIGN, 2002.
- 5 Bodurka-Beyers D, Morris M, Eifel PJ, Levenback C, Beyers MW, Lucas KR, et al. Posttherapy surveillance of women with cervical cancer: an outcomes analysis. *Gynecol Oncol* 2000;78:187-93.
- 6 Hong JH, Tsai CS, Lai CH, Chang TC, Wang CC, Chou HH, et al. Recurrent squamous cell carcinoma of cervix after definitive radiotherapy. *Int J Radiat Oncol Biol Phys* 2004;60:249-57.
- 7 Lim KCK, Howells REJ, Evans AS. The role of clinical follow up in early stage cervical cancer in south Wales. *BJOG* 2004;111:1444-8.
- 8 Slevin M, Nichols SE, Downer SM, Wilson P, Lister TA, Amott S, et al. Emotional support for cancer patients: what do patients really want? *Br J Cancer* 1996;74:1275-9.
- 9 NHMRC National Breast Cancer Centre and National Cancer Control Initiative. *Clinical practice guidelines for the psychosocial care of adults with cancer*. Australia, NSW: NHMRC, 2003.
- 10 Downing A, Mikeljevic JS, Haward B, Forman D. Variation in the treatment of cervical cancer patients and the effect of consultant workload on survival: a population-based study. *Eur J Cancer* 2007;43:363-70.