Resource document for LHBs, Trusts and their MDTs

Gynaecological cancer follow up: evidence for efficacy of interventions in surveillance

October 2013
(review date October 2014)

The Cancer Delivery Plan aims to ensure that all interventions used in the NHS are effective. As part of this, the Cancer National Specialist Advisory Group has developed summaries of the existing evidence for interventions during the follow-up phase to aid organisations when developing their local follow-up strategies.

Follow-up aims to fulfil a number of purposes, including, but not limited to, surveillance for recurrence or metastasis of the original disease.

It is important that the design of follow-up strategies takes into account the holistic needs of people following a diagnosis of cancer and advice on those wider aspects are being developed elsewhere.

This document is intended as a neutral collation of the evidence regarding whether an intervention makes a difference to the clinical management of a patient in relation to surveillance, to act as a resource for local teams.

We have not undertaken systematic literature reviews, but have included the evidence that the cancer NSAG considers relevant. This includes where there is evidence that an intervention is not effective. The document does not attempt to recommend a particular pathway or the mechanism of interventions (e.g. Consultant versus CNS or Outpatient appointment versus telephone).

Unfortunately the evidence base surrounding follow-up is relatively poor, and it is important to remember that a lack of evidence of effectiveness does not equate to evidence of non-effectiveness.

The following summaries therefore represent the collective view of the appropriate site-specific groups regarding what evidence is currently available on the effectiveness of medical interventions for surveillance.

**Gynaecological cancers**

**Relevant current guidance:**


NICE have not produced guidelines that include gynaecological cancers, however Scotland have produced guidance through their equivalent process:


Recently published papers and results of trials:

Note: a) not an exhaustive list, b) presented in publication date order, c) Identified post November 2011 (publication date for the most recent guideline above – South Wales Network Guideline)

None identified

Trials awaiting results

None identified
Appendix A

Follow Up for Gynaecological Cancers

Status of this document: Advice to the Cancer Implementation Group Patient Centred Care Sub Group from the Cancer National Specialist Advisory Group for Gynaecological Cancers Sub Group

Date: November 2011 (revised August 2013)

Purpose: To advise on the key clinical components for gynaecological cancers

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# Table of Contents

Resource document for LHBs, Trusts and their MDTs

Gynaecological cancer follow up: evidence for efficacy of interventions in surveillance

October 2013

Appendix A

Follow up for Gynaecological Cancers

Background

Role of follow up

What needs to be defined?

Evidence base

Current guidance

Current changes to follow up

References

Appendix A1

The OV05 study

Appendix A2

1. Extracts from the All Wales Guidelines on the Management of Gynaecological Cancers (2001)

Cervical Cancer

Ovarian Cancer

Endometrial Cancer

Vulval Cancer

2. Extract from the DRAFT South Wales guidelines (may be subject to change)

Recommended follow up protocol for cervical, endometrial, ovarian and vulval cancers

3. Extracts from the North Wales guidelines

Cervical Cancer

Ovarian cancer

Endometrial Cancer
Follow up for Gynaecological Cancers

Background

Traditionally, all patients who have been diagnosed with a gynaecological cancer have been followed up for at least five years by the medical team in the hospital where they had treatment. With more individuals surviving a diagnosis of cancer and increasing incidence due to an ageing population, current models of follow up are, however, unsustainable. For gynaecological cancer, although the rates of cervical cancer are falling, endometrial cancer incidence is increasing year on year. Overall survival for endometrial cancer is also good, meaning that most women will be eligible for the full five years of the follow up protocol.

In keeping with other tumour sites, there is a general lack of evidence for follow up after gynaecological cancers, and most recommendations are based on expert opinion (evidence level 5). Therefore, although there exists published advice on follow up at local, regional, national and international levels, no standard protocols exist and follow up protocols frequently lack detail regarding what constitutes an ideal follow up consultation. An example of advice is the European Society for Medical Oncology (ESMO) guideline on follow up after endometrial cancer which addresses the main issues but, as the authors state, is clearly lacking in an evidence base:1

Most recurrences will occur within the first 3 years after treatment, and 3- to 4-monthly evaluations with history, physical and gynecological examination are usually recommended. Follow-up intervals of 6 months are recommended during the fourth and fifth years, and annually thereafter. No impact on survival of a routine follow-up strategy has been demonstrated. However, since a significant number of relapses occur isolated in the vagina or pelvis, early detection and possibly curative treatment of these should be the main focus of follow-up. Routine technical examinations such as PAP smears or imaging studies are of unproven benefit.

Role of follow up

Historically, follow up has been based around the detection of recurrent disease as in the preceding example, but there is now increasing emphasis on other survivorship issues, and the aims of follow up therefore include:

1) Detection of recurrence
2) Management of symptoms related to side effects of treatment (e.g. menopausal symptoms, radiation toxicity etc.)
3) Psychological support
4) Psychosexual support

With regard to management of symptoms related to side effects of treatment, of note is the newly formed SPIRIT (South Wales Pelvic Radiotherapy Toxicity) Group which is a multispecialty team which has come together recently to improve the investigation and management of patients who have gastrointestinal symptoms following radiotherapy. The group was formed after a well-attended meeting in Swansea in May 2012 which was organised by interested clinicians in conjunction with the South Wales Cancer Network and WAGE (Welsh Association of Gastroenterology and Endoscopy). The SPIRIT Group has forged links with a patient group, the Pelvic Radiation Disease Association. The SPIRIT Group has identified gastroenterologists in several hospitals in South Wales who are prepared to take a lead in seeing and treating these patients.

There is relevant practice guidance and an algorithm from the Royal Marsden Hospital on how to investigate (both are referenced in the introductory section of this document and available on the WAGE website www.wage.org.uk).


These developments fit in with the gynae NSAG’s view that survivorship and quality of life are key components of follow up and are important for cancer units as well as cancer centres, particularly because cancer follow up takes place in both cancer units and cancer centres and includes many patients who have had a full course of whole pelvic radiotherapy as part of their adjuvant or definitive treatment.

What needs to be defined?

It is becoming clearer that the following need to be addressed for each tumour site:

1) What is the aim of follow up?
2) What should be done at each follow up?
3) Who should perform follow up?
4) Where should follow up be performed?
5) How frequently should follow up be performed?

With regard to who should perform follow up, although much of the follow up for gynaecological cancer is currently performed by doctors, it is clear that specialist nurses can provide excellent follow up. Of relevance to the increasing focus on survivorship issues, two recent developments in the South Wales Cancer Network are the setting up of a nurse-led survivorship clinic in ovarian cancer and a nurse-led psychosexual clinic, both in the Velindre Cancer Centre.

Evidence base

As previously mentioned, there is a lack of evidence for most of the follow up performed after gynaecological cancer. However, there is equally little evidence to say that stopping follow up is safe. There is one randomised study however which has changed practice; the OV05 study looking at the role of CA125 measurement in ovarian cancer. Details of this study are in Appendix 1, but in summary no benefit was found from routinely measuring the CA125 in
women who had been treated for ovarian cancer. Women who had routine measurement of CA125 received chemotherapy earlier and had a worse quality of life than those who received chemotherapy based on symptoms. The authors concluded that it was safe to omit routine CA125 measurement in these women. However, if investigation and treatment are to be based purely on the occurrence of symptoms, it is important that women have early access to CT scanning and chemotherapy, which can not be always guaranteed to be the case.

Current guidance

Documents in Wales that give advice on follow up are:

1) The All Wales Guidelines on the Management of Gynaecological Cancers
2) The South Wales Network Guidelines for Gynaecological Cancers (currently in draft form)
3) The North Wales Network Guidelines for Gynaecological Cancers

Extracts from these documents are listed in Appendix 2.

Current changes to follow up

The South East Wales Gynaecological Network recently agreed a change to follow up meaning that women with endometrial cancer are followed up with their local gynaecologist. This has the advantage of less travelling time for patients.

Velindre Cancer Centre is planning to utilise skills mix and involve Specialist Nurses in the follow up of particularly ovarian plus other gynaecological cancer patients.

References

2) OV05 A randomised trial in relapsed ovarian cancer: early treatment based on CA125 levels alone vs delayed treatment based on conventional clinical indicators. Rustin et al. ASCO Conference 2009

Appendix A1

The OV05 study
Traditionally, CA125 tumour marker has been measured in all patients during follow up for ovarian cancer. Recently, data have been presented from the MRC OV05 study (Rustin et al. ASCO Conference 2009) which looked at early treatment of relapsed ovarian cancer based on CA125 alone versus delayed treatment based on conventional clinical indicators. CA125 was measured every three months following complete remission after first line treatment for ovarian cancer. If the result was raised more than 2 x upper limit of normal the patient was randomised between disclosure of the results or not.

Of 1442 patients registered, only 529 were randomised. The main reasons for non-randomisation were: relapse without CA125 rising; non-relapse and withdrawal from the study.

The results showed that those whose CA125 was disclosed had second-line chemotherapy on average 4.8 months sooner and third line chemotherapy 4.6 months sooner than those in the delayed arm. The overall survival was no different between the two arms. Moreover the early chemotherapy group had a worse quality of life, with a 2.6 month difference in time from randomisation to first deterioration in quality of life.

The authors concluded that women can be reassured that there is no benefit from early detection of relapse by routine CA125 measurement and that even if CA125 rises, chemotherapy can be delayed until signs or symptoms of recurrence occur. Moreover they state that women can be offered informed choices in follow up between routine CA125 measurement or not. This decision can be facilitated by discussion with their oncologist and can take into account other factors such as response to first line treatment and access to imaging.

Appendix A2


Cervical Cancer

As patients who relapse locally have a good chance of cure and/or prolonged remission with prompt treatment, the patient should be followed up by trained personnel when the earliest signs and symptoms of recurrence will be recognised. Follow up should be at a combined clinic. Follow up intervals are currently arbitrary and would be subject to audit and review. The following schedule is suggested (C):

- Three monthly the first year.
- Six monthly the second years.
- Annual review until five years.

Ovarian Cancer

There is no evidence indicating that routine follow-up in patients with ovarian carcinoma influences survival. At present follow-up should consist of:
Recommended follow up protocol for cervical, endometrial, ovarian and vulval cancers

\[^{1}\] Changed from published wording by the Gynaecological NSAG due to concerns about appropriateness
Patients should be advised regularly about:
- the aims of the FU appointments
- their key worker and central contact (e.g. CNS/consultant secretary)
- presenting early with suspicious symptoms
- the method and schedule of FU
- late complications from surgery and radiotherapy

The following follow up regimen is recommended:

- First year – every 3 months
- Second year – every 6 months
- Third, Fourth and Fifth year – annually

Consider discharge after 5 years for cervical and ovarian cancer patients (who have not recurred). Vulval cancer patients have field changes within their perineum and are at risk of long term recurrences or new primaries therefore are followed up for life.

There is no role for routine cytology or radiology apart from baseline imaging for ovarian cancer and post treatment MRI for cervical cancer patients who underwent chemoradiotherapy.

Patients should be examined vaginally and abdominally at each visit.

NB In view of the post treatment morbidity associated with cervical and vulval cancer patients, they should be followed up in the cancer centres unless there are specific reasons for referring back to the original unit. The ovarian cancer patients generally have a higher recurrence rate and therefore would benefit from central follow up in order to reduce any delays of diagnosing recurrences.

3. Extracts from the North Wales guidelines

Cervical Cancer

Careful inspection and palpation of the vaginal vault and palpation for any pelvic masses should be performed 3 monthly for 2 years, 6 monthly for 1 year and then annually.

Hospital follow up should be for 5 years. Vault cytology is not helpful if the patient has had radiotherapy. Cervical cytology is necessary if the cervix has been conserved for early disease or after trachelectomy.

All patients must be encouraged to report any symptoms suggestive of recurrent disease immediately by contacting their CNS rather than wait until their next outpatient appointment.

Psychosexual, emotional, bowel, genitourinary, neuropraxia other problems may need detailed discussion with the clinical nurse specialist and psychological, lymphoedema, pain, spiritual and other support services.
Ovarian cancer

Careful inspection and palpation of the vaginal vault and palpation for any pelvic masses should be performed 3 monthly for 2 years, 6 monthly for 1 year and then annually.

Hospital follow up should be for 5 years. A prospective questionnaire study of 948,576 women and subsequent meta-analysis showed that with a mean of 5.3 years follow up, current use of HRT was associated with an increased incidence and death from ovarian cancer. The effect was seen in serous histology only and included borderline tumours. A non significant increased risk was seen with increased duration of use. Previous use of the combined pill did not attenuate this effect. Also past users of HRT were not at increased risk. This effect was such that over 5 years 1 extra ovarian cancer was seen in 2500 users and 1 extra cancer death per 3300 users. HRT should not be offered to women with serous carcinoma but women with serous borderline tumours should be fore-warned of a slight increased risk of recurrence of borderline disease should they choose to use HRT (grade B recommendation; Million Women Study Collaborators, 2007). Vaginal vault or cervical cytology is not required unless coincident CIN. Patients will need genetic counselling if other family members have had ovarian or other relevant cancers.

All patients must be encouraged to report any symptoms suggestive of recurrent disease immediately by contacting their CNS rather than wait until their next outpatient appointment.

Recently reported evidence in abstract form has not revealed a benefit for routine CA125 testing and treatment of relapse at asymptomatic elevation in comparison to treatment at onset of symptoms (OV05/ EORTC 55955; Rustin and van der Burg, 2009). Patients with an asymptomatic elevated CA125 (2x above normal) were treated 5 months earlier and were retreated for second relapse 5 months earlier in a randomised trial of 1442 women having had debulking surgery and first line chemotherapy with a normal CA125 at the end of treatment. Overall survival and quality of life was equivalent in both groups. Women should decide for themselves whether or not they wish routine CA125 testing as part of their follow up management or only when they develop new symptoms (Evidence level 1b; grade A recommendation).

Psychosexual, emotional, bowel, genitourinary, neuropraxia other problems may need detailed discussion with the clinical nurse specialist and psychological, lymphoedema, pain, spiritual and other support services.

Endometrial Cancer

The value of clinical follow up is debatable. There is no evidence that an earlier detection of recurrence leads to an improved survival. However careful inspection and palpation of the vaginal vault and palpation for any pelvic masses should be performed 3 monthly for 2 years, 6 monthly for 1 year and then annually.

Hospital follow up should be for 5 years. Vaginal vault cytology is not helpful.

All patients must be encouraged to report any symptoms suggestive of recurrent disease immediately by contacting their CNS rather than wait until their next outpatient appointment.
Psychosexual, emotional, bowel, genitourinary, neuropraxia other problems may need detailed discussion with the clinical nurse specialist and psychological, lymphoedema, pain, spiritual and other support services.

Vulval Cancer

As patients who relapse locally with vulval carcinoma have a good chance of cure and/or prolonged remission with prompt re-treatment, the patient should be followed up in an environment where trained personnel are available to recognise the earliest signs or symptoms of recurrence at the cancer centre or unit.

Follow up should be performed 3 monthly for 2 years, 6 monthly for 1 year and then annually.

All patients must be encouraged to report any symptoms suggestive of recurrent disease immediately by contacting their CNS rather than wait until their next outpatient appointment.

Psychosexual, emotional, bowel, genitourinary, neuropraxia other problems may need detailed discussion with the clinical nurse specialist and psychological, lymphoedema, pain, spiritual and other support services.