Complete Summary

GUIDELINE TITLE

Follow-up after primary therapy for endometrial cancer: a clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Fung-Kee-Fung M, Dodge J, Elit L, Lukka H, Chambers A, Oliver T, Gynecology Cancer Disease Site Group. Follow-up after primary therapy for endometrial cancer. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jan 10. 26 p. (Evidence-based series; no. 4-9). [31 references]

GUIDELINE STATUS

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Endometrial cancer

GUIDELINE CATEGORY

Management
Risk Assessment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the most appropriate strategy for the follow-up of patients with endometrial cancer who are clinically disease-free after receiving potentially curative primary treatment

Specifically, to evaluate differences in follow-up intervals, diagnostic interventions, clinical setting or specialty, that may influence patient outcomes related to local or distant recurrence, survival, or quality of life

TARGET POPULATION

Women without evidence of disease after primary, potentially curative treatment for any stage of endometrial cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Patient counseling on potential symptoms of recurrence
2. General examination, including complete history and pelvic-rectal examination for:
    - Patients at low risk of recurrence
    - Patients of high risk of recurrence
3. Counseling on adverse effects of radiotherapy

Interventions and practices considered but not recommended include Pap smear, chest x-ray, abdominal ultrasound, computed tomography (CT), and CA 125 testing.

MAJOR OUTCOMES CONSIDERED

- Disease recurrence rates
- Local or distant recurrence
- Survival
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature was searched using MEDLINE (OVID: 1980 through October 2005), EMBASE (OVID: 1980 through October 2005), the Cochrane Library (OVID: Issue 3, 2005), the Canadian Medical Association Infobase, and the National Guideline Clearinghouse. In addition, the proceedings of the meetings of the American Society of Clinical Oncology (1999-2005), and the American Society for Therapeutic Radiology and Oncology (1999-2003) were searched for relevant abstracts. Reference lists of papers that were eligible for inclusion in the systematic review were scanned for additional citations.

The literature search of the electronic databases combined disease specific terms (uterine neoplasms/ or cervical neoplasms/ or endometrial neoplasms/ or (cervix or endometrium or endometrial and cancer or carcinoma)) and (surveillance.ti. or follow$.ti.or strategy.ti. or routine.ti.) for the following study designs: practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, non-randomized comparative cohort studies, prospective single-cohort studies, and retrospective single-cohort studies.

Study Selection Criteria

Articles were selected for inclusion in the evidence series if they reported data on follow-up strategies for patients who had received curative treatment for endometrial cancer and who were clinically disease-free at study point. Specifically, studies were to describe the follow-up program, define the entry criteria for the study population, and report outcome data on survival, the number of recurrences found during screening, or on patient preferences. Case reports, letters, editorials, and papers published in a language other than English were not considered for inclusion in the systematic review of the evidence.

In the absence of randomized controlled trials, in order of preference, comparative cohort studies, prospective single-cohort studies, and retrospective single-cohort studies were deemed eligible for inclusion. Practice guidelines, meta-analyses, or systematic reviews explicitly based on evidence related to the guideline question were also eligible for inclusion in the systematic review.

NUMBER OF SOURCE DOCUMENTS

Sixteen non-comparative retrospective studies provided the evidence basis for this report. In addition, two systematic reviews were also identified.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Synthesizing the Evidence

The recurrence rates of the non-comparative trials were pooled using the formula pooled recurrence rate (PRR) = $\sum(w_i RR_i) / \sum w_i$, where PRR is the pooled recurrence rate of the studies, w_i is the weight of the i^{th} study, and RR_i is the response rate of the i^{th} study. RR was calculated by dividing the number of recurrences by the total number of patients in a study. 'w' was determined by the inverse of the variance for a study, with the variance calculated by multiplying the proportion of patients with a recurrence by the proportion of patients with no recurrence, and then dividing the result by the total number of patients in the study. The 95% confidence interval (95%CI) for each PRR was calculated by the formula PRR ± $1.96SE_{PRR}$, where $SE_{PRR} = \sqrt{(1/\sum w_i)}$.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This systematic review was developed by Cancer Care Ontario's Program in Evidence-based Care (PEBC). Evidence was selected and reviewed by members of the PEBC Provincial Gynecology Cancer Disease Site Group and methodologists.

The body of evidence in the review is comprised of retrospective data. That evidence, combined with expert consensus, forms the basis of a clinical practice guideline developed by the Provincial Gynecology Cancer Disease Site Group.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner Feedback

Practitioner feedback was obtained through a mailed survey of 172 practitioners in Ontario (101 family practitioners, 40 medical oncologists, 16 surgeons, 14 gynecologists, and 1 urologist). The survey consisted of items evaluating the methods, results, and interpretive summary. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Gynecology Disease Site Group (DSG) reviewed the results of the survey.

Report Approval Panel

The evidence series was circulated to the two members of the Report Approval Panel and the Guidelines Coordinator of the Program in Evidence-based Care (PEBC). Feedback was provided by the Panel and the Coordinator and is summarized below. Feedback was reviewed by the Gynecology Cancer DSG and modifications were made to the series in response. The revised draft was then recirculated back to the Panel for final approval.

Peer Review

The systematic review was submitted to the Journal of Gynecologic Oncology in November 2005. In December 2005, feedback requiring substantive revisions was provided by the Journal. Feedback was reviewed by the Gynecology Cancer DSG and modifications were made to the series in response. A revised manuscript was then re-submitted to the journal for consideration in January 2006.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

There is a lack of randomized controlled trial evidence related to the clinical questions. Based on the interpretation of evidence from retrospective studies and expert consensus opinion, the Gynecology Cancer Disease Site Group recommends the following:

- It is recommended that all patients receive counselling about the potential symptoms of recurrence of endometrial cancer, because the majority of recurrences in the identified studies were symptomatic.
    - Symptomatic signs of possible recurrence can include, but are not limited to, unexplained vaginal bleeding or discharge, detection of a mass, abdominal distension, persistent pain, especially in the abdomen or pelvic region, fatigue, diarrhoea, nausea or vomiting, persistent cough, swelling, or weight loss.

- The most appropriate follow-up strategy is likely one based upon the risk of recurrence with individual patient preferences for more or less follow-up taken into account.
    - For patients at a surgically or pathologically confirmed low risk of recurrence (i.e., stage IA or IB, grade 1 or 2): A general examination, including a complete history and a pelvic-rectal examination, conducted semi-annually or annually for the first three years, and annually for the next two years.
    - For patients at high risk of recurrence (i.e., stage IA or IB, grade 3, or stage IC or advanced stage). A general examination, including a complete history and a pelvic-rectal examination, every three to six months for the first three years and semi-annually for the next two years.
- Since the majority of patients with recurrence were symptomatic and virtually all recurred within five years, it seems reasonable that patients return to annual population-based general physical and pelvic examination after five years of recurrence-free follow-up.
- There is insufficient evidence to inform the optimum clinical setting or type of specialist required for follow-up however, it is recommended that all patients be followed by a health care professional who is knowledgeable about the natural history of the disease, and who is comfortable performing speculum and pelvic exams, in order to diagnose or detect a local (vaginal) recurrence.
    - If a patient is initially followed by a specialist, it seems reasonable that they be followed by a qualified general practitioner after three to five years of recurrence-free follow-up.
- It is recommended that all patients undergo a targeted investigation to rule out recurrence if symptomatic, since patients with local recurrence are potentially curable with further therapy.
- There is insufficient evidence to inform the routine use of Pap smear, chest x-ray, abdominal ultrasound, computed tomography (CT) scan or CA 125 testing to detect asymptomatic recurrences.
- Where treatment with radiotherapy is involved, it is recommended that patients be counselled on the potential adverse effects of radiotherapy. Adverse effects associated with radiotherapy can include complications with the rectum, urinary bladder, vagina, skin, subcutaneous tissue, bones, etc.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by non-comparative retrospective studies.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- In 12 studies, overall (local and distant) recurrence rates ranged from 8% to 19% with a weighted mean of 13% (95% confidence interval [CI]; 11%-14%). In four studies that categorized patients by risk of recurrence, recurrence rates ranged from 1% to 3% for low-risk patients and 5% to 16% for high-risk patients.
- In 12 studies, 41% to 100% of all recurrences were symptomatic; the weighted mean being 77% (95% CI; 74 to 81%).
- In 9 studies 68 to 100% of recurrences occurred within approximately three years of follow-up.
- The number of asymptomatic patients with recurrences detected by a routine follow-up test alone was not consistently reported, however with the available data, as a percentage of total recurrences:
    - Seven studies reported 5% to 33% of recurrences were detected by physical examination
    - Four studies reported 0% to 4% of recurrences were detected by Pap smear
    - Six studies reported 0% to 14% of recurrences were detected by chest x-ray
    - Two studies reported 4% and 13% of recurrences were detected by abdominal ultrasound
    - Two studies reported 5% and 21% of recurrences were detected by computed tomography (CT) scan
    - One study reported 15% of recurrences in selected patients were detected by CA 125 level.

POTENTIAL HARMS

Adverse effects associated with radiotherapy can include complications with the rectum, urinary bladder, vagina, skin, subcutaneous tissue, bones, etc.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the evidence-based series is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding their content or use or application and disclaims any for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Jan 10

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Gynecology Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Gynecology Cancer Disease Site Group (DSG) disclosed potential conflict of interest information. There were no conflicts of interest declared among the Disease Site Group members.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Follow-up after primary therapy for endometrial cancer: a clinical practice guideline. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2006 Jan. Various p. (Practice guideline; no. 4-9). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 5, 2006. The information was verified by the guideline developer on June 1, 2006.

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