Complete Summary

GUIDELINE TITLE

Adjuvant care for stage 1 ovarian cancer.

BIBLIOGRAPHIC SOURCE(S)

Gynecology Cancer Disease Site Group. Elit L, Fyles A, Chambers A, Fung Kee Fung M, Covens A, Carey M. Adjuvant care for stage I ovarian cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 May 3. 33 p. (Practice guideline report; no. 4-13). [62 references]

GUIDELINE STATUS

This is the current release of the guideline.

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

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SCOPE

DISEASE/CONDITION(S)

Stage I ovarian cancer

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Obstetrics and Gynecology
Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To evaluate the role of adjuvant care in women with completely surgically staged stage I ovarian cancer
- To evaluate the role of adjuvant care in women who receive incomplete or no surgical staging of ovarian cancer
- To evaluate the optimal strategy for adjuvant care in women with ovarian cancer

TARGET POPULATION

Women with newly diagnosed stage I ovarian cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

1. Node sampling versus pelvic and para-aortic node dissection
2. Adjuvant radiotherapy versus no radiotherapy
3. Adjuvant chemotherapy versus no chemotherapy
4. Adjuvant chemotherapy versus radiotherapy
5. Adjuvant chemotherapy versus intraperitoneal radioactive chromic phosphate
6. Whole abdominal radiation versus pelvic radiation and chemotherapy
7. Combination chemotherapy

MAJOR OUTCOMES CONSIDERED

- Survival (overall, disease-free, and recurrence-free)
- Recurrence rate
- Adverse events

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

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

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE (1965 through May 2003), CANCERLIT (1975 through October 2002), and the Cochrane Library (2003, Issue 1) databases were searched. "Neoplasms, ovarian" (Medical subject heading [MeSH]) was combined with each of the following terms: "early stage" or "stage I," "chemotherapy" (MeSH), "surgery" (MeSH), and "radiotherapy" (MeSH). These terms were then combined with the search terms for the following study designs and publication types: practice guidelines, systematic reviews, meta-analyses, reviews, randomized controlled trials, and controlled clinical trials. The Canadian Medical Association Infobase (http://mdm.ca/cpgsnew/cpgs/index.asp) and the National Guideline Clearinghouse (http://www.guideline.gov) were searched for existing evidence-based practice guidelines. Relevant articles and abstracts were selected and reviewed by three reviewers, and the reference lists from these sources were searched for additional trials, as were the reference lists from relevant review articles.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they were fully published reports or published abstracts of randomized controlled trials (RCTs) comparing two or more adjuvant setting treatments (chemotherapy, radiotherapy, and/or surgery) in women with stage I ovarian cancer.

NUMBER OF SOURCE DOCUMENTS

Eight practice guidelines or consensus statements and 25 published randomized controlled trials were reviewed.

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 of Randomized Controlled Trials
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The practice guideline outlines randomized controlled trials (RCTs) that included stage I patients. There have been major methodological concerns with some of these studies, and attention will be drawn to those areas (i.e., inclusion of patients in stage II and III with minimal residual disease). Only those studies where the information on outcome of stage I patients can be determined will be included in the final analysis.

To estimate the overall effect on survival of the treatments for early stage ovarian cancer, mortality data (the number of patients who had died during the study and the number of patients included in the survival analysis by the investigators) were abstracted from the published reports of individual randomized controlled trials and pooled using the Review Manager software (RevMan 4.1) provided by the Cochrane Collaboration (Metaview © Update Software). Only stage I results were pooled in the analysis; thus, only studies that separated the results for stage I patients were included in the analysis. Combining data in this manner assumes a constant hazard ratio of risks for the groups being compared. Results are expressed as relative risks (also known as risk ratios) with 95% confidence intervals (CI), where a relative risk (RR) for mortality less than one indicates that the experimental treatment improved survival compared with the control treatment. Conversely, a relative risk greater than one suggests that patients in the control group experienced lower mortality. The relative risk is calculated by taking the ratio of the proportion of patients who have died in the experimental treatment group to the proportion of patients who have died in the control group. The random-effects model was used for comparative testing of the pooled results across studies in preference to the fixed-effects model, as the more conservative estimate of effect.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Gynecology Cancer Disease Site Group agreed that adjuvant chemotherapy should include a platinum-based regimen. There was no consensus concerning the use of single versus combination treatment.

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 96 practitioners in Ontario (39 medical oncologists, 19 radiation oncologists, 17 surgeons, four

pathologists, and 17 gynecologists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations above should be approved as a practice guideline. Written comments were invited. The practitioner feedback survey was mailed out on September 5, 2003. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Gynecology Cancer Disease Site Group (DSG) reviewed the results of the survey.

Approval Process

The practice guideline report was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. Seven of 12 members of the PGCC returned ballots. Five PGCC members approved the practice guideline report as written and two members approved the guideline conditional on the Gynecology Cancer DSG addressing specific concerns.

The Gynecology Cancer DSG revised the recommendations based on the suggestions offered by the PGCC member. Final approval of the original guideline report was obtained from the Gynecology Cancer DSG and the PGCC.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- The stage of ovarian cancer is an important prognostic factor that influences survival and the choice of therapy. The quality of the surgical staging is a key determinant of treatment recommendations.
- Women who have undergone optimal surgical staging, including pelvic and para-aortic lymph node sampling, and have stage I disease may or may not benefit from adjuvant platinum-based chemotherapy (see "Qualifying Statements" field).
- Women who have not undergone optimal surgical staging can be offered two options. The first option is that they undergo reoperation to optimally define the tumour stage and then be offered adjuvant therapy based on the findings. The other option is that they be offered platinum-based chemotherapy to decrease the risk of recurrence and improve survival.
- There is insufficient evidence to make a recommendation on the role of adjuvant pelvic radiation, whole abdominal-pelvic radiotherapy, or intraperitoneal radioactive chromic phosphate.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by practice guideline/consensus statements, randomized controlled trials, and meta-analyses.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved understanding of the role of adjuvant care in women with completely surgically staged stage 1 ovarian cancer and in women who receive incomplete or no surgical staging
- Increased familiarity with optimal strategies for adjuvant care in women with ovarian cancer

POTENTIAL HARMS

The most frequently reported adverse effects associated with chemotherapy were grade 3 or 4 vomiting/nausea and grade 3 or 4 leukopenia.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Accurate staging and tumour histology information is essential for developing recommendations on the management of ovarian cancer. A tumour pathology causing doubt should be reviewed by an expert.
- The standard of care for stage IA and IB grade I ovarian cancer in Ontario has been surgical resection with optimal staging and no adjuvant therapy. This standard is based on the work by Young et al involving non-optimally staged, stage I cancer and the prognostic studies by Vergote et al that reported an extremely low probability of recurrence in this population.
- The results of the largest trial comparing adjuvant chemotherapy to no chemotherapy in women with early stage ovarian cancer (International Collaborative Ovarian Neoplasm Study/Adjuvant ChemoTherapy In Ovarian Neoplasm [ICON/ACTION] Trial) are controversial because:
    - A subgroup analysis of the ACTION Trial showed no benefit from adjuvant chemotherapy in women who underwent optimal surgical staging, but that analysis was underpowered.
    - The entry criteria for the ICON Trial were vague and did not reflect the standard of surgical care offered in Canadian centres.
    - The meta-analysis included in this practice guideline demonstrates that stage I patients have an improved outcome with adjuvant chemotherapy. However, an estimated 90% of women undergoing surgical resection for ovarian cancer do not undergo optimal surgical staging. If the restaging of a suboptimally staged patient reveals a more advanced disease, chemotherapy is the preferred treatment option. If reoperation confirms stage I disease, there is insufficient evidence for or against adjuvant chemotherapy. The treatment decision must be based on a discussion with the patient about potential benefits and risks.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the practice

guideline 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 warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility 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

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

2004 May 3

GUIDELINE DEVELOPER(S)

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

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), 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

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.

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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 is available:

- Adjuvant care for stage 1 ovarian cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2004 May 3. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RS, 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 NGC summary was completed by ECRI on September 23, 2004. The information was verified by the guideline developer on October 20, 2004.

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