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Neoadjuvant or Adjuvant Therapy for Resectable Gastric Cancer Practice Guideline Report #2-14

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ORIGINAL GUIDELINE: December 2000
MOST RECENT LITERATURE SEARCH: May 12, 2003
NEW EVIDENCE ADDED TO THE GUIDELINE REPORT: May 21, 2003

New evidence found by update searches since completion of the original guideline is consistent with the original recommendations.

SUMMARY

Guideline Question

Should patients with resectable gastric cancer (T1-4,N0-2,M0) receive neoadjuvant or adjuvant therapy in addition to surgery?

Target Population

These recommendations apply to adult patients with potentially curable surgically resected (T1-4,N0-2,M0) gastric cancer.

Recommendation

- Following surgical resection, patients whose tumours penetrated the muscularis propria or involved regional lymph nodes should be considered for adjuvant combined chemoradiotherapy. The current standard protocol consists of one cycle of 5-FU (425 mg/m²/day) and leucovorin (20 mg/m²/day) in a daily regimen for five days, followed one month later by 4,500 cGy (180 cGy/day) of radiation given with 5-FU (400 mg/m²/day) and leucovorin (20 mg/m²/day) on days 1 through 4 and the last three days of radiation. One month after completion of radiation, two cycles of 5-FU (425 mg/m²/day) and leucovorin (20 mg/m²/day) in a daily regimen for five days are given at monthly intervals.
- There is no evidence on which to make a recommendation for patients with node-negative tumours that have not penetrated the muscularis propria.
- For patients unable to undergo radiation, adjuvant chemotherapy alone may be of benefit, particularly for patients with lymph node metastases. The optimal regimen remains to be defined.
- There is insufficient evidence from randomized trials to recommend neoadjuvant chemotherapy, or neoadjuvant or adjuvant radiation therapy or immunotherapy, either alone or in combination, outside of a clinical trial.

Qualifying Statements

- Patients should understand the tradeoffs between survival benefit and toxicity before making treatment decisions.

Methods

Entries to the MEDLINE database (1966 through April 2003), CANCERLIT (1983 to October 2001), and the Cochrane Library database of Systematic Reviews (2003, Issue 1) and abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology and the American Society for Therapeutic Radiology and Oncology were systematically searched for evidence relevant to this practice guideline report.

Evidence was selected and reviewed by two members of the Practice Guidelines Initiative Gastrointestinal Cancer Disease Site Group and methodologists. This practice guideline report has been reviewed and approved by the Gastrointestinal Cancer Disease Site Group, which comprises medical oncologists, radiation oncologists, surgeons, a pathologist, and two patient representatives.

External review by Ontario practitioners was obtained through a mailed survey. Final approval of the practice guideline report was obtained from the Practice Guidelines Coordinating Committee.

The Practice Guidelines Initiative has a formal standardized process to ensure the currency of each guideline report. This process consists of periodic review and evaluation of the scientific literature and, where appropriate, integration of this literature with the original guideline information.

Key Evidence

- A large intergroup trial has confirmed statistically significant improvement in overall and relapse-free survival with adjuvant combined chemoradiotherapy. Compared to surgery alone, overall survival at three years was improved by 9% (50% versus 41%, $p=0.005$), and relapse-free survival was increased from 31% to 48%, $p=0.001$ [two-sided log-rank test] in the chemoradiotherapy group. At five years, adjuvant chemo-radiotherapy increased overall survival by 11.6% (40% versus 28.4%), and improved relapse-free survival from 25% to 38%, $p<0.001$ [two-sided log-rank test] compared to surgery alone.
- With respect to adjuvant chemotherapy alone, three literature-based meta-analyses of randomized trials detected modest benefits, particularly in lymph node-positive patients.
- Randomized trials of neoadjuvant chemotherapy, or neoadjuvant or adjuvant radiotherapy or immunotherapy have thus far failed to detect a consistent benefit for these treatments compared with surgery alone.

For further information about this practice guideline report, please contact: Dr. Jean Maroun, Chair, Gastrointestinal Cancer Disease Site Group, Ottawa Regional Cancer Centre, General Division, 503 Smyth Road, Ottawa, Ontario, K1H 1C4; TEL (613) 737-7000, ext. 6708; FAX (613) 247-3511.

*The Practice Guidelines Initiative is sponsored by:
Cancer Care Ontario & the Ontario Ministry of Health and Long-term Care.*

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PREAMBLE: About Our Practice Guideline Reports

The Practice Guidelines Initiative (PGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multidisciplinary Disease Site Groups of the PGI using the methodology of the Practice Guidelines Development Cycle.¹ The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis, and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee (PGCC), whose membership includes oncologists, other health providers, patient representatives, and Cancer Care Ontario executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

Reference:

¹ 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.

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