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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Management of malignant pleural effusion.

Bibliographic Source(s)

Alberta Provincial Lung Tumour Team. Management of malignant pleural effusion. Version 1. Edmonton (AB): CancerControl Alberta; 2014 Oct. 13 p. (Clinical practice guideline; no. LU-010). [27 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The Alberta Provincial Lung Tumour Team has adapted the recommendations from the British Thoracic Society and the American College of Chest Physicians, with modifications to fit the Alberta context (see the "Adaptation" field).

Key Points

- All treatment decisions should be guided by patient preferences.
- Selection of a treatment approach is largely dependent on the patient's anticipated duration of survival and the availability/appropriate utilization of local resources.

1. The management of a malignant pleural effusion (MPE) should be individualized and may sometimes need to be discussed at a multidisciplinary Tumour Board.
2. The management of a MPE is palliative and therefore all treatment decisions should consider the type of malignancy (e.g., lung versus ovarian), patients' symptoms, life expectancy, functional status, quality of life, and goals of therapy.
    a. Palliative therapy goals should improve patients' quality of life through:
        - Relief of dyspnea
        - The need for reintervention
        - Reduced hospitalizations and length of stay

Diagnostic and Baseline Investigations

3. All patients with a suspected MPE should have an initial clinical history and physical examination. An MPE should be considered as a cause of breathlessness in patients with diagnosed cancer.
4. A chest radiograph should be used to detect the presence of a pleural effusion. A lateral decubitus chest radiograph may be used to differentiate pleural liquid from pleural thickening.
5. Computerized tomography (CT) scans, when clinically indicated, can detect very small pleural effusions (less than 10 mL of fluid); intravenous administration of iodinated contrast material is recommended. A thoracic ultrasound can also be used to investigate small pleural effusions.
6. Undiagnosed effusions of more than 1 cm from the chest wall on a lateral decubitus chest radiograph should be diagnostically evaluated by ultrasound-assisted thoracentesis. Patients known to have advanced cancer do not need thoracentesis for small asymptomatic effusions.
7. If a thoracentesis is going to be performed, all effusions should be sent for cytology if a patient does not have a diagnosis of a MPE.
    a. A minimum 50mL to 60 mL of pleural fluid should be withdrawn for analysis.
    b. The fluid should be analyzed for cell count and differential, gram stain and culture, pH, and glucose, as well as protein and lactate dehydrogenase (LDH), which can help to ascertain whether the fluid is a transudate or an exudate using Light's Criteria.
    c. Consider sending larger volumes of fluid (100 mL to 200 mL) for cell block and molecular testing (e.g., *epidermal growth factor receptor [EGFR]*).
8. All patients with a diagnosed MPE should be referred to respiratory medicine or thoracic surgery although initial thoracentesis should not be delayed in symptomatic patients. In Edmonton, referrals can be made to the Alberta Thoracic Oncology Program, and in Calgary/Southern Alberta, to the Tom Baker Cancer Centre Dyspnea clinic.
9. Availability of clinical resources should allow rapid assessment (within 1 week) of referred patient in order to avoid unnecessary emergency room visits and hospitalizations.
10. Chest ultrasonography, if available, is recommended at the point of care for any thoracentesis or percutaneous chest drain placement (including indwelling pleural catheter [IPC]).

<u>Asymptomatic Patients</u>

11. Asymptomatic patients do not require treatment but should be observed as MPEs may become symptomatic and require palliative treatment. Patients with a large MPE may be considered for a therapeutic thoracentesis.

<u>Symptomatic Patients</u>

12. Patients with symptoms may be considered for an initial therapeutic thoracentesis to relieve symptoms prior to further invasive treatments. The recommended total amount of fluid removed per session is 1000 mL to 1500 mL although clinician judgment may be used to remove more if chest symptoms and/or pleural pressure are monitored. In some cases significantly less fluid should be removed if the patient develops chest discomfort or tightness during drainage or if pleural pressures decrease below -20 cmH_20. The rate of reaccumulation of the pleural effusion, the patient's clinical and symptomatic response, and prognosis will help to guide the subsequent choice of therapy.
13. Outpatient therapeutic thoracentesis alone may occasionally be indicated for patients with a prognosis less than 1 month, and/or a poor performance status (PS), and/or a slow reaccumulation of the pleural effusion (i.e., more than 1 month) and should be performed as required to control symptoms.
14. Patients should be considered for more definitive interventions after the first or second thoracentesis. Treatment options include:
    a. Indwelling (i.e., tunneled) pleural catheter
        - Consider for patients with trapped lung who experience at least partial symptom relief following thoracentesis, or those with a shorter anticipated survival
        - Consider for any patient with a preference to avoid hospitalization and initial discomfort of pleurodesis
    b. Talc pleurodesis via thoracoscopy:
        - Consider for patients with a longer anticipated survival
        - Consider if patient does not want indwelling catheter for lifestyle reasons
        - Contraindicated for patients with an irremediably entrapped or trapped lung
    c. Talc pleurodesis via chest tube:
        - Indicated for patients with a longer anticipated survival or contraindication to thoracoscopy
        - Contraindicated for patients with an irremediably entrapped or trapped lung
15. The source of talc should be taken into consideration when selecting a treatment option. In Alberta, uncertainty with currently available talc preparations has resulted in more frequent use of IPCs.
16. Chemotherapy may be considered as an adjunct treatment option. In particular, patients undergoing first line systemic treatment for tumours with typically rapid response rates (e.g., small cell lung cancer and lymphoma) may avoid the above definitive treatments.
17. Coordination with a palliative care team is recommended for patients with incomplete response to initial treatment.

Follow-up

18. All patients treated with an IPC should be managed and followed-up in the context of a specialist clinic, where accessible, such as the Dyspnea Clinic (Calgary) or Alberta Thoracic Oncology Program (ATOP) (Edmonton).

Clinical Algorithm(s)

An algorithm titled "Treatment Algorithm" is provided in the original guideline document.

Scope

Disease/Condition(s)

Malignant pleural effusion (MPE)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Oncology

Pulmonary Medicine

Radiology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To outline treatment recommendations for patients with a malignant pleural effusion (MPE)

Target Population

Adults over the age of 18 years with malignant pleural effusions (MPEs)

Note: Different principles may apply to pediatric patients and patients with different types of cancer.

Interventions and Practices Considered

Diagnosis/Evaluation

1. Initial clinical history and physical examination
2. Chest radiograph to detect the presence of a pleural effusion (including lateral decubitus chest radiograph)
3. Computerized tomography (CT) scans if indicated, with intravenous administration of iodinated contrast material
4. Thoracic ultrasound
5. Ultrasound-assisted thoracentesis
6. Cytological examination of pleural fluid, including cell count and differential, gram stain and culture, pH, glucose, protein, and lactate dehydrogenase (LDH)
7. Cell block and molecular testing of pleural fluid
8. Referral to respiratory medicine or thoracic surgery of all patients with diagnosed malignant pleural effusion (MPE)
9. Chest ultrasonography (point of care for any thoracentesis or percutaneous chest drain placement [including indwelling pleural catheter (IPC)])

Treatment/Management

1. Observation of asymptomatic patients, with consideration of therapeutic thoracentesis for patients with large MPEs
2. Initial therapeutic thoracentesis to relieve symptoms prior to further invasive treatments
3. Outpatient therapeutic thoracentesis alone
4. Indwelling (i.e., tunneled) pleural catheter
5. Talc pleurodesis via thoracoscopy
6. Talc pleurodesis via chest tube
7. Adjunctive chemotherapy
8. Coordination with a palliative care team
9. Follow-up of patients treated with an IPC

Major Outcomes Considered

- Mean survival
- Complications/side effects of treatment
- Symptom relief (dyspnea, chest pain or heaviness, dry cough)
- Quality of life
- Length of hospital stay
- Recurrence
- Sensitivity and specificity of diagnostic tests

Methodology

Methods Used to Collect/Select the 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

Guideline Questions

- What diagnostic and baseline investigations are recommended for patients with suspected or confirmed malignant pleural effusions (MPEs)?
- What are the recommended treatment options for patients with asymptomatic MPEs?
- What are the recommended treatment options for patients with recurrent symptomatic MPEs?
- What is the recommended follow-up after treatment for a MPE?

Search Strategy

PubMED, MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews electronic databases were searched to March 27, 2014 for literature on the management of MPEs. The following search terms were used: *pleural effusion, malignant* (MeSH [Medical Subject Heading]); results were limited to literature published since 2009, human subjects (19+ years), published in English, clinical trials, guidelines, meta-analysis, practice guidelines, randomized controlled trials (RCTs), and systematic reviews. Reference lists were scanned for relevant literature. Articles not accessible through the library system were excluded.

The National Guideline Clearinghouse (NGC) was also searched for guidelines on MPEs, as well as other prominent guideline developer websites.

Number of Source Documents

- MEDLINE
  - Results: 16
  - Relevant: 11
- EMBASE
  - Results: 0
  - Relevant: 0
- PubMed
  - Results: 41
  - Relevant: 26 (includes 9 duplicates from previous searches)
- Cochrane Database of Systematic Reviews
  - Results: 2 (including a protocol for an upcoming review due in early 2015 and a withdrawn review)
  - Relevant: 0

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Lung Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the GURU Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org/) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial Lung Tumour Team with input from members of the Respiratory Health Strategic Clinical Network. Members of the Alberta Provincial Lung Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, respirologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Lung Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the GURU Handbook (see the "Availability of Companion Documents' field).

Formulating Recommendations

The working group members formulate the guideline recommendations based on the evidence synthesized by the KM Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the GURU Handbook, the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the GURU does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

- A recent cost-effectiveness analysis of managing malignant pleural effusions (MPEs) found that indwelling pleural catheterization (IPC) was the most cost-effective and least expensive option overall in comparison to thoracentesis and pleurodesis, although cost was dependent on the patient's length of survival. For patients with longer survival, pleurodesis was the most cost-effective treatment option given the cost of replenishing treatment supplies and ongoing home care for IPC therapy versus hospital-based pleurodesis.
- Based on the results of one cost-effectiveness study, treatment with talc pleurodesis was less costly than IPC with similar effectiveness. IPC became more cost effective when life expectancy was 6 weeks or less. Using data from a recent randomized control trial (RCT) comparing IPC with talc pleurodesis found no significant difference in mean cost of managing patients with IPC versus talc pleurodesis. However, for patients with limited survival (less than 14 weeks) IPC was significantly less expensive than talc pleurodesis.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Guideline Review and Approval

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations were adapted from British Thoracic Society and American College of Chest Physicians guidelines, with modifications to fit the Alberta context. See the "Adaptation" field.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of malignant pleural effusion (MPE) resulting in improvement in global health status, quality of life, and dyspnea

Potential Harms

- The recommended total amount of fluid removed per session of thoracentesis is 1000 mL to 1500 mL although clinician judgment may be used to remove more if chest symptoms and/or pleural pressure are monitored. In some cases significantly less fluid should be removed if the patient develops chest discomfort or tightness during drainage or if pleural pressures decrease below -20cmH20. Thoracentesis is associated with a small risk of re-expansion pulmonary edema, which occurs in approximately 1 percent of patients, but it is independent of the volume of fluid removed, pleural pressures, and pleural elastance.
- Indwelling pleural catheter (IPC) requires a regular outpatient drainage schedule, which may be burdensome for the patient or caregiver, therefore, patient preferences must be considered when balancing the requirements for hospitalization in the case of pleurodesis versus IPC in an ambulatory and outpatient setting. Complications from IPCs are uncommon. One multicentre study of 1,021 malignant pleural effusion (MPE) patients reported an infection rate of 5 percent from IPCs, of which 54 percent could be treated with antibiotics without removal of the catheter. A systematic review of IPC safety found that both serious and minor complications were rare and that their use was without complications in 87.5 percent of patients. Specifically, the following complications were reported: empyema (2.8 percent), pneumothorax requiring a chest tube (5.9 percent), unspecified pneumothorax (3.9 percent), cellulitis (3.4 percent), obstruction/clogging (3.7 percent), and unspecified catheter malfunction (9.1 percent).
- The most common adverse events associated with talc pleurodesis are fever, pain, and gastrointestinal symptoms; less common complications include arrhythmia, dyspnea, respiratory failure, systemic inflammatory responses, empyema, and talc dissemination.
- Consider patient and caregiver/family acceptability of an intervention, cost, and avoidance of invasive procedures and complications that remove the patient from their home and disrupt the course of their terminal cancer.

Contraindications

Contraindications

- Talc pleurodesis via thoracoscopy is contraindicated for patients with an irremediably entrapped or trapped lung.
- Talc pleurodesis via chest tube is contraindicated for patients with an irremediably entrapped or trapped lung.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Lung Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial Lung Tumour Team. Management of malignant pleural effusion. Version 1. Edmonton (AB): CancerControl Alberta; 2014 Oct. 13 p. (Clinical practice guideline; no. LU-010). [27 references]

Adaptation

The recommendations were adapted from the following British Thoracic Society and American College of Chest Physicians guidelines, with modifications to fit the Alberta context:

- Roberts ME, Neville E, Berrisford RG, Antunes G, Ali NJ, BTS Pleural Disease Guideline Group. Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010. Thorax. 2010 Aug;65 Suppl 2:ii32-40.
- Simoff MJ, Lally B, Slade MG, Goldberg WG, Lee P, Michaud GC, Wahidi MM, Chawla M. Symptom management in patients with lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e455S-97S.

Date Released

2014 Oct

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

Guideline Committee

Alberta Provincial Lung Tumour Team

Composition of Group That Authored the Guideline

Members of the Alberta Provincial Lung Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, dermatologists, nurses, pathologists, and a pharmacist, methodologist, and Knowledge Management Specialist.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Lung Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Lung Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available in from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Version 2. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Available from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 5, 2015. The information was verified by the guideline developer on October 22, 2015.

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