Evidence-based Series 7-11 Version 2

A Quality Initiative of the
Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)

The Management of Thymoma:
Guideline Recommendations

Members of the Lung Disease Site Group

Report Date: June 18, 2014

An assessment conducted in December 2016 deferred the review of Evidence-based Series (EBS) 7-11 Version 2, which means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol).

Evidence-based Series (EBS) 7-11, consists of four sections:
Section 1: Guideline Recommendations
Section 2: Evidentiary Base or Systematic
Section 3: EBS Development Methods
and External Review Process
Section 4: Guideline Review and Summary Tool

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Guideline Report History

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A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: April 10, 2008

These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Review Summary and Tool for a summary of updated evidence published between 2006 and 2013, and for details on how this Clinical Practice Guideline was ENDORSED.

CLINICAL QUESTION
What is the optimal management of thymoma?

TARGET POPULATION
Adult patients with locally advanced, unresectable, and recurrent thymoma (excluding thymic carcinoma and carcinoids).

RECOMMENDATIONS
The following recommendations for the management of thymoma by surgery, radiotherapy and systemic therapy were developed through a combination of systematic review of the medical literature and a formal consensus process by members of the Thymoma Consensus Group which includes Thymoma Working Group members, other members of the Provincial Lung Disease Site Group, and other experts from across Canada (see Section 2 for details).
CONSENSUS RECOMMENDATIONS FOR THE MANAGEMENT OF THYMOMA

Stage I

Surgery
1. Complete surgical resection of the entire thymus gland, including all mediastinal tissues anterior to the pericardium, aorta, and superior vena cava from phrenic nerve to phrenic nerve laterally and from the diaphragm inferiorly to the level of the thyroid gland superiorly, including the upper poles of the thymus, is recommended as the standard of care.
2. For resection of thymoma, an open median sternotomy surgical approach is recommended.
3. Minimally invasive approaches (e.g., video-assisted thoracic surgery [VATS]) are not considered the standard of care and are not recommended at this time.

Radiotherapy
4. Neither postoperative nor neoadjuvant radiotherapy is recommended for stage I disease.

Systemic Therapy
5. Neither postoperative nor neoadjuvant systemic therapy is recommended for stage I disease.

Medically Inoperable Stage I Disease
6. Chemoradiation or radiation alone should be considered for patients who are medically unfit for surgery.

Stage II

Surgery
7. Complete surgical resection (as outlined for stage I) is the usual practice and is the recommended standard of care.
8. For resection of thymoma, an open median sternotomy surgical approach is recommended.
9. Minimally invasive approaches (e.g., VATS) are not considered the standard of care and are not recommended at this time.

Radiotherapy
10. Routine adjuvant radiation is currently not recommended. Radiation should be considered in patients with high risk for local recurrence. These risk factors include invasion through the capsule, close surgical margins, WHO grade B type, and tumour adherent to pericardium.
11. Radiotherapy (RT) has risks for acute and long-term toxicity, notably a risk for the development of secondary malignancies (1) and coronary heart disease (2). Possible risks and benefits need to be discussed with patients, particularly in younger individuals.

Systemic Therapy
12. Neither postoperative nor neoadjuvant systemic therapy is recommended for stage II disease.

Medically Inoperable Stage II Disease
13. Chemoradiation or radiation alone should be considered for patients who are medically unfit for surgery.

Stage III

14. Patients presenting with locally advanced or metastatic disease should be carefully evaluated for multimodality therapy that includes neoadjuvant chemotherapy, surgical resection or adjuvant postoperative chemoradiotherapy.
Resectable or Potentially Resectable Stage III Disease

Surgery
15. For stage IIIA, surgery should be considered either initially or following neoadjuvant therapy, with the aim being complete removal of the tumour with wide surgical margins. In stage IIIB, patients should be assessed for surgery following neoadjuvant chemoradiotherapy.

16. If at thoracotomy complete resection is not found to be possible, maximal debulking (with appropriate vascular reconstruction) should be undertaken. clips should be placed to mark residual tumour for adjuvant radiation. If it is apparent prior to surgery that complete resection may not be feasible, neoadjuvant chemoradiation should be considered prior to surgery.

17. Bilateral phrenic nerve resection is not recommended because of the severe respiratory morbidity that results.

Neoadjuvant Radiotherapy and Systemic Therapy
18. Neoadjuvant chemoradiotherapy is widely used in this setting.
   ▪ The data supporting this standard is not yet established.

19. The optimal neoadjuvant therapy regimen for minimizing operative morbidity and mortality, and maximizing resectability and survival rates is not yet established.
   ▪ Cisplatin-based combination chemotherapy regimens are recommended as reasonable options.

20. The optimal sequencing of radiotherapy and chemotherapy is not yet established.
   ▪ If treatment volumes are small, concurrent chemoradiotherapy is recommended as a reasonable option.
   ▪ If the initial tumour volume is considered to be too bulky, sequential therapy, with chemotherapy followed by radiation therapy, is recommended as a reasonable option. Resection may be performed prior to radiotherapy.

21. To establish the diagnosis of thymoma, either a computerized tomography (CT) -guided core-needle biopsy or an open surgical biopsy should be performed, prior to considering neoadjuvant therapy.

Adjuvant Radiotherapy and Systemic Therapy
22. Adjuvant radiotherapy is widely used in this setting and is recommended. Adjuvant chemotherapy may be a consideration.

Unresectable Stage III Disease
23. Where surgery is inappropriate, chemotherapy concurrent with, or sequential to, radiation therapy is recommended.

24. The definition of unresectable disease is debated, and may vary with surgical expertise, but is generally defined as extensive tumour involving middle mediastinal organs such as the trachea, great arteries, and/or heart that does not respond to cisplatin-based combination chemotherapy.

Stage IVA
25. The recommendations established for stage III disease are applicable to stage IVA cases as well. The following are notable modifications or exceptions to this:
Resectable or Potentially Resectable Stage IVA Disease

Surgery
26. Surgery should be considered either initially or following neoadjuvant therapy, with the aim being complete removal of the tumour with wide surgical margins. Surgery is recommended only if pleural and pericardial metastases can be resected.

Neoadjuvant Radiotherapy and Systemic Therapy
27. Neoadjuvant chemoradiotherapy is an option in this setting.
28. Cisplatin-based combination chemotherapy regimens are reasonable options.

Adjuvant Radiotherapy and Systemic Therapy
29. Adjuvant chemoradiotherapy is an option.

Unresectable Stage IVA Disease
30. Where surgery is not feasible because of extensive or technically unresectable pleural or pericardial metastases, chemotherapy is commonly provided. Chemotherapy concurrent with, or sequential to, radiation therapy is also an option.
31. In stage IVA, unresectable disease may include extensive bilateral and/or pleural-based disease, pericardial metastases, or extrathoracic metastases.

Stage IVB
32. These types of thymoma are extremely rare, and generic recommendations are not possible.

Surgery
33. Not applicable

Radiotherapy
34. Radiotherapy may be appropriate, particularly for life-threatening situations.

Systemic Therapy
35. Cisplatin-based combination chemotherapy is an appropriate option.
36. Octreotide, alone or in combination with a corticosteroid, may be a reasonable option for recurrent cases.

Recurrent Disease.

Surgery
37. Surgical resection should be considered in patients with a localized recurrence after apparently successful initial therapy. In some patients with stage IV disease, the resection of isolated pleural metastases is an appropriate initial approach. For cases with multiple pleural metastases, chemotherapy, with or without subsequent surgery, is often appropriate.

Radiotherapy
38. Radiotherapy may be appropriate either alone or in combination with chemotherapy.

Systemic Therapy
39. Cisplatin-based chemotherapy may be an appropriate therapy either alone or as part of combined chemoradiotherapy.
40. Octreotide, alone or in combination with a corticosteroid, may be a reasonable option.
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REFERENCES
