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

Surgical, Radiation, and Systemic Treatments of Patients with Thymic Epithelial Tumours

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An assessment conducted in November 2025 deferred the review of Guideline 7-11 Version 3. This 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)

Guideline 7-11 Version 3 comprises 5 sections. You can access the summary and full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/736

Section 1:	**Recommendations Summary**
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Surgical, Radiation, and Systemic Treatments of Patients with Thymic Epithelial Tumours

This is a quick reference guide and provides the guideline recommendations only. For key evidence associated with each recommendation, the systematic review, and the guideline development process, see the Full Report.

GUIDELINE OBJECTIVES

The objective of this guideline is to determine the most effective therapy for patients with thymic epithelial tumours.

TARGET POPULATION

The target population are adult patients with thymic epithelial tumours, including thymoma, thymic carcinoma, and thymic neuroendocrine tumours (NETs).

INTENDED USERS

The intended users of this guideline are all healthcare professionals managing patients with thymic epithelial tumours.

DEFINITIONS

Complete resection – refers to an R0 resection of the tumour or resection with negative margins

Total resection – refers to resection of the entire thymus (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), the tumour, and any involved structures

Partial resection – refers to resection of less than the entire thymus, but includes the tumour and any involved structures

RECOMMENDATIONS

The staging system for patients with thymic epithelial tumours has recently changed to a TNM staging system [1,2]. The evidence used to support these recommendations was mainly from observational studies that used the prior Masaoka and Masaoka-Koga staging systems [3,4]. Given the lack of randomized trials, the Working Group endorsed most of the consensus-based recommendations from the previous version of this guideline [5] (see Appendix 1). For patients with thymic NETS, recommendations were endorsed from the National Comprehensive Cancer Network (NCCN) Version 1.2021 Neuroendocrine and Adrenal Tumors Guideline [6].

General Principles
1. The aim of surgery in all cases is to achieve a complete resection.
2. The TNM staging system should be used for all patients.
3. Discussion of all patients at multidisciplinary cancer conference (MCC) is strongly recommended, not just at local MCC but also with higher-volume centres. Presentation at the International Thymic Malignancies Interest Group tumour board should be considered.

PATIENTS WITH THYMOMA

THYMOMA TNM 8th edition Stage I (T1aN0M0/T1bN0M0) (Encapsulated or unencapsulated, with or without extension into mediastinal fat / Extension into mediastinal pleura)

Surgery

1. Total resection is preferred over partial resection, especially for patients with myasthenia gravis (MG).
2. Open or minimally invasive approaches (e.g., video-assisted thoracic surgery [VATS] or robot-assisted thoracoscopic surgery [RATS]) are both recommended as the standard of care.

Radiotherapy

3. Neoadjuvant radiotherapy is not recommended.
4. Postoperative radiotherapy (PORT) is not routinely recommended.

Systemic Therapy

5. Neither neoadjuvant nor adjuvant systemic therapy is recommended.

Medically Inoperable Stage I Disease

6. Radiotherapy could be considered for patients who are medically unfit for surgery.

THYMOMA TNM 8th edition Stage II (T2N0M0) (Invasion of pericardium)

Surgery

7. Total resection is preferred over partial resection, especially for patients with MG.
8. Open or minimally invasive approaches (e.g., VATS or RATS) are both recommended as the standard of care.

Radiotherapy

9. Neoadjuvant radiotherapy is not recommended.
10. Routine PORT is currently not recommended. However, PORT should be considered in patients with incomplete resection or positive margins. Radiotherapy has risks for acute and late toxicities. Late toxicities such as cardiac disease and secondary malignancies may be more relevant in younger patients. Possible harms versus benefits need to be discussed with patients.

Systemic Therapy

11. Neither neoadjuvant nor adjuvant systemic therapy is recommended.

Medically Inoperable Stage II Disease

12. Radiotherapy could be considered for patients who are medically unfit for surgery.

THYMOMA TNM 8th edition Stage III (T3N0M0/T4N0M0) (Involvement of lung, brachiocephalic vein, superior vena cava, chest wall, phrenic nerve, hilar [extrapericardial] pulmonary vessels / Involvement of aorta, arch vessels, main pulmonary artery, myocardium, trachea, or esophagus)

13. Patients presenting with locally advanced disease should be carefully evaluated for multimodality therapy.

Resectable or Potentially Resectable Stage IIIa Disease

Surgery

14. Surgery should be considered either initially or following neoadjuvant therapy, with the aim being total removal of the tumour with clear surgical margins.
15. Total resection is preferred over partial resection, especially for patients with MG.
16. Open thymectomy is recommended as the standard of care. Minimally invasive approaches are not recommended as the standard of care.
17. If at initial surgery there are concerns about clear resection margins, clips should be placed to mark areas at risk to guide PORT. If it is apparent prior to surgery that complete resection may not be feasible, neoadjuvant chemotherapy or chemoradiotherapy should be considered prior to surgery.
18. Unilateral phrenic nerve resection is acceptable. Bilateral phrenic nerve resection is contraindicated because of the severe respiratory morbidity that results.

Neoadjuvant Systemic Therapy and Radiotherapy

19. The decision to give neoadjuvant therapy should be discussed at an MCC. Options include neoadjuvant chemotherapy (with possible PORT) or concurrent chemoradiotherapy. Histological confirmation of diagnosis is recommended prior to any therapy.

20. 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 is a reasonable option.

PORT and Adjuvant Systemic Therapy

21. PORT could be offered if the patient has not received neoadjuvant radiotherapy.
22. Adjuvant chemotherapy is not routinely recommended and should not be offered without discussion at MCC.

Unresectable Stage III Disease

23. The distinction between resectable and unresectable disease is controversial and patients with suspected unresectable stage III disease should be discussed at an MCC for consideration for referral to a high-volume tertiary thoracic surgical centre.
24. Where surgery is not feasible, chemotherapy concurrent with, or sequential to, radiotherapy is recommended.

THYMOMA TNM 8th edition Stage IVa (TanyN1M0/TanyN0M1a/TanyN1M1a) (Involvement of anterior [perithymic] nodes / separate pleural or pericardial nodule(s) / anterior [perithymic] nodes, Separate pleural or pericardial nodule(s))

25. Patients should all be discussed at an MCC and be evaluated for multimodality therapy.

Resectable or Potentially Resectable Stage IVa Disease

Surgery

26. Surgery should be considered either initially or following neoadjuvant therapy, with the aim being total removal of all tumour with clear surgical margins. Surgery is recommended only if pleural and pericardial metastases can be resected.
27. Total resection is preferred over partial resection, especially for patients with MG.
28. Open thymectomy is recommended as the standard of care. Minimally invasive approaches are not recommended as the standard of care.
29. If at initial surgery there are concerns about clear resection margins, clips should be placed to mark areas at risk to guide PORT. If it is apparent prior to surgery that complete resection may not be feasible, neoadjuvant chemotherapy or chemoradiotherapy should be considered prior to surgery.
30. Unilateral phrenic nerve resection is acceptable. Bilateral phrenic nerve resection is contraindicated because of the severe respiratory morbidity that results.

Neoadjuvant Systemic Therapy

31. Neoadjuvant chemotherapy is an option in this setting.
32. 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 is a reasonable option.

PORT and Adjuvant Systemic Therapy

33. PORT should be offered if the patient has not received neoadjuvant radiotherapy.
34. Adjuvant chemotherapy is not routinely recommended and should not be offered without discussion at an MCC.

Unresectable Stage IVa Disease

35. The distinction between resectable and unresectable disease is controversial and patients with suspected unresectable stage IVa disease should be discussed at an MCC for consideration for referral to a high-volume tertiary thoracic surgical centre.
36. Where surgery is not feasible, chemotherapy can be considered. Chemotherapy can be given concurrent with, or sequential to, radiotherapy.

THYMOMA TNM 8th edition Stage IVb (TanyN2M0/TanyN2M1a/TanyNanyM1b) (Involvement of deep intrathoracic or cervical nodes / deep intrathoracic or cervical nodes, Separate pleural or pericardial nodule(s) / pulmonary intraparenchymal nodule or distant organ metastasis)

37. This is a heterogeneous group of patients and treatment decisions should reflect the extent and location of metastatic disease. Generic recommendations are not possible. These patients should be discussed at an MCC, and treatment goals reviewed. Treatment options include chemotherapy (platinum-based recommended; there is insufficient evidence to recommend the routine use of other systemic agents), radiotherapy, and potential surgery.

THYMOMA Recurrent Disease

38. These patients should be discussed at an MCC, and multimodality therapy should be considered.

Surgery

39. Resection should be considered in patients with intrathoracic disease. This should be considered as part of multimodality care.

Radiotherapy

40. Radiotherapy may be appropriate either alone or as part of multimodality care.

Systemic Therapy

41. Cisplatin-based chemotherapy may be an appropriate therapy either alone or as part of multimodality care. There is insufficient evidence to recommend the routine use of other systemic agents.

PATIENTS WITH THYMIC CARCINOMA

THYMIC CARCINOMA TNM 8th edition Stage I (T1aN0M0/T1bN0M0) (Encapsulated or unencapsulated, with or without extension into mediastinal fat / Extension into mediastinal pleura)

Surgery

1. Total resection is preferred over partial resection.
2. Open thymectomy is recommended as the standard of care.

Radiotherapy

3. Neoadjuvant radiotherapy is not recommended.
4. PORT may be considered.

Systemic Therapy

5. Neoadjuvant chemotherapy is not recommended.
6. Adjuvant chemotherapy is not routinely recommended.

Medically Inoperable Stage I Disease

7. Radiotherapy could be considered for patients who are medically unfit for surgery. There is insufficient evidence regarding the role of chemotherapy.

THYMIC CARCINOMA TNM 8th edition Stage II (T2N0M0) (Invasion of pericardium)

Surgery

8. Total resection is preferred over partial resection.
9. Open thymectomy is recommended as the standard of care.

Radiotherapy

10. Neoadjuvant radiotherapy is not recommended.
11. PORT should be considered. Possible harms versus benefits need to be discussed with patients.

Systemic Therapy

12. Neoadjuvant chemotherapy is not recommended.
13. Adjuvant chemotherapy is not routinely recommended.

Medically Inoperable Stage II Disease

14. Radiotherapy could be considered for patients who are medically unfit for surgery. There is insufficient evidence regarding the role of chemotherapy.

THYMIC CARCINOMA TNM 8th edition Stage III (T3N0M0/T4N0M0) (Involvement of lung, brachiocephalic vein, superior vena cava, chest wall, phrenic nerve, hilar [extrapericardial] pulmonary vessels / Involvement of aorta, arch vessels, main pulmonary artery, myocardium, trachea, or esophagus)

15. Patients presenting with locally advanced disease should be carefully evaluated for multimodality therapy.

Resectable or Potentially Resectable Stage IIIa Disease

Surgery

16. Surgery should be considered either initially or following neoadjuvant therapy, with the aim being total removal of the tumour with clear surgical margins.
17. Total resection is preferred over partial resection.
18. Open thymectomy is recommended as the standard of care.

19. If at initial surgery there are concerns about clear resection margins, clips should be placed to mark areas at risk to guide PORT. If it is apparent prior to surgery that complete resection may not be feasible, neoadjuvant chemotherapy or chemoradiotherapy should be considered prior to surgery.
20. Unilateral phrenic nerve resection is acceptable. Bilateral phrenic nerve resection is contraindicated because of the severe respiratory morbidity that results.

Neoadjuvant Systemic Therapy and Radiotherapy

21. The decision to give neoadjuvant therapy should be discussed at an MCC. Options include neoadjuvant chemotherapy (with possible PORT) or concurrent chemoradiotherapy. Histological confirmation of diagnosis is recommended prior to any therapy.
22. 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 is a reasonable option.

PORT and Adjuvant Systemic Therapy

23. PORT should be offered if the patient has not received neoadjuvant radiotherapy.
24. Adjuvant chemotherapy should be considered based on representation at MCC if the patient did not have neoadjuvant chemotherapy.

Unresectable Stage III Disease

25. The distinction between resectable and unresectable disease is controversial and patients with suspected unresectable stage III disease should be discussed at an MCC for consideration for referral to a high-volume tertiary thoracic surgical centre.
26. Where surgery is not feasible, chemotherapy concurrent with, or sequential to, radiotherapy is recommended.

THYMIC CARCINOMA TNM 8th edition Stage IVa (TanyN1M0/TanyN0M1a/TanyN1M1a) (Involvement of anterior [perithymic] nodes / separate pleural or pericardial nodule(s) / anterior [perithymic] nodes, Separate pleural or pericardial nodule(s))

27. Patients should all be discussed at an MCC and be evaluated for multimodality therapy.

Resectable or Potentially Resectable Stage IVa Disease

Surgery

28. Surgery should be considered either initially or following neoadjuvant therapy, with the aim being total removal of all tumour with clear surgical margins. Surgery is recommended only if pleural and pericardial metastases can be resected.
29. Total resection is preferred over partial resection.
30. Open thymectomy is recommended as the standard of care.
31. If at initial surgery there are concerns about clear resection margins, clips should be placed to mark areas at risk to guide PORT. If it is apparent prior to surgery that complete resection may not be feasible, neoadjuvant chemotherapy or chemoradiotherapy should be considered prior to surgery.
32. Unilateral phrenic nerve resection is acceptable. Bilateral phrenic nerve resection is contraindicated because of the severe respiratory morbidity that results.

Neoadjuvant Systemic Therapy

33. Neoadjuvant chemotherapy is recommended in this setting.
34. 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 is a reasonable option.

PORT and Adjuvant Systemic Therapy

35. PORT should be offered if the patient has not received neoadjuvant radiotherapy.
36. Neoadjuvant chemotherapy is the preferred option.

Unresectable Stage IVa Disease

37. The distinction between resectable and unresectable disease is controversial and patients with suspected unresectable stage IVa disease should be discussed at an MCC for consideration for referral to a high-volume tertiary thoracic surgical centre.
38. Where surgery is not feasible, chemotherapy concurrent with, or sequential to, radiotherapy is recommended.

THYMIC CARCINOMA TNM 8th edition Stage IVb (TanyN2M0/TanyN2M1a/TanyNanyM1b) (Involvement of deep intrathoracic or cervical nodes / deep intrathoracic or cervical nodes, Separate pleural or pericardial nodule(s) / pulmonary intraparenchymal nodule or distant organ metastasis)

39. This is a heterogeneous group of patients and treatment decisions should reflect the extent and location of metastatic disease. Generic recommendations are not possible. These patients should be discussed at an MCC, and treatment goals reviewed. Treatment options include chemotherapy (platinum-based recommended; there is insufficient evidence to recommend the routine use of other systemic agents), radiotherapy, and potential surgery.

THYMIC CARCINOMA Recurrent Disease

40. These patients should be discussed at an MCC, and multimodality therapy should be considered.

Surgery

41. Resection should be considered in patients with intrathoracic disease. This should be considered as part of multimodality care.

Radiotherapy

42. Radiotherapy may be appropriate either alone or as part of multimodality care.

Systemic Therapy

43. Cisplatin-based chemotherapy may be an appropriate therapy either alone or as part of multimodality care. There is insufficient evidence to recommend the routine use of other systemic agents.

PATIENTS WITH THYMIC NEUROENDOCRINE TUMOURS
(endorsed from the NCCN Version 1.2021 Neuroendocrine and Adrenal Tumors Guideline [6])

THYMIC NEUROENDOCRINE TUMOURS Localized disease (Stage I-II)

Surgery

1. Total resection is preferred over partial resection.
2. Open thymectomy is recommended as the standard of care.

THYMIC NEUROENDOCRINE TUMOURS Resectable locoregional disease (Stage IIIA/B)

Surgery

3. Total resection is preferred over partial resection.
4. Open thymectomy is recommended as the standard of care.

Incomplete resection and/or positive margins with low grade (typical carcinoid)

5. Consider observation, or
   Consider radiotherapy

Incomplete resection and/or positive margins with intermediate grade (atypical carcinoid)

6. Consider observation, or
   Consider radiotherapy ± cytotoxic chemotherapy. Chemoradiation is thought to have most efficacy for tumours with atypical histology or tumours with higher mitotic and proliferative indices (e.g., Ki-67). Cytotoxic chemotherapy options include cisplatin + etoposide, or carboplatin + etoposide.

THYMIC NEUROENDOCRINE TUMOURS Locally unresectable locoregional disease (Stage IIIA/B)

7. For symptom control, consider addition of focal therapy (i.e., endobronchial therapy debulking, ablation).

Primary therapy

Low grade (typical carcinoid)

8. Observation (if asymptomatic), or
   Octreotide or lanreotide (if somatostatin receptor [SSR]-positive and/or hormonal symptoms), or
   Everolimus, or
   Temozolomide ± capecitabine, or
   Radiotherapy

Intermediate grade (atypical carcinoid)

9. Observation (if asymptomatic and non-progressive), or
   Radiotherapy ± concurrent cisplatin + etoposide or carboplatin + etoposide (chemoradiation is thought to have most efficacy for tumours with atypical histology or tumours with higher mitotic and proliferative indices [e.g., Ki-67]), or
   Cytotoxic chemotherapy with cisplatin + etoposide, or temozolomide ± capecitabine, or
   Octreotide or lanreotide (if SSR-positive and/or hormonal symptoms), or
   Everolimus

Subsequent therapy

10. If disease progression, treatment with octreotide or lanreotide should be discontinued for non-functional tumours and continued in patients with functional tumours; those regimens may be used in combination with any of the subsequent options.
11. Clinical trial (preferred), or
    Consider changing therapy if progression on first-line therapy, or
    Consider peptide receptor radionuclide therapy with 177Lu-dotatate (if SSR-positive and progression on octreotide/lanreotide).

THYMIC NEUROENDOCRINE TUMOURS Metastatic disease (Stage IV)

12. For symptom control, consider addition of focal therapy (i.e., endobronchial therapy debulking, ablation).
13. NETs are highly heterogeneous, and all elements need to be considered (e.g., burden of disease, symptoms, histopathology, rate of growth) when determining the best course of treatment.

Asymptomatic, low tumour burden and low grade (typical carcinoid)

14. Observe (chest computed tomography [CT] with contrast and abdominal/pelvic multiphasic CT or magnetic resonance imaging every 3-6 months) or octreotide or lanreotide (if SSR-positive and/or hormonal symptoms).

Clinically significant tumour burden and low grade (typical carcinoid) or evidence of disease progression or intermediate grade (atypical carcinoid) or symptomatic disease

15. Clinical trial (preferred), or
    Observation, in select patients (observation can be considered if asymptomatic or for tumours on the lower end of the spectrum), or
    Octreotide or lanreotide (if SSR-positive and/or hormonal symptoms), or
    Everolimus, or
    Peptide receptor radionuclide therapy with 177Lu-dotatate (if SSR-positive and progression on octreotide or lanreotide), or
    Cisplatin + etoposide or carboplatin + etoposide or temozolomide ± capecitabine (can be considered for intermediate-grade/atypical tumours with Ki-67 proliferative index and mitotic index in the higher end of the defined spectrum), or
    Liver-directed therapy for liver-predominant disease
16. Consider changing therapy if progression on first-line therapy. If disease progression, treatment with octreotide or lanreotide should be discontinued for non-functional tumours and continued in patients with functional tumours; those regimens may be used in combination with any of the subsequent options.

IMPLEMENTATION CONSIDERATIONS

The Working Group members believed that patients in rural areas or patients who are disadvantaged may find it more challenging to attend daily PORT treatments or treatments in

high-volume centres since they may live further away from these centres in Ontario or may have difficulty in acquiring transportation for daily treatments than patients in urban areas or patients who are less disadvantaged. Also, peptide receptor radionuclide therapy has not been approved for patients with thymic epithelial tumours in Ontario.

FURTHER RESEARCH

Larger, collaborative, international prospective trials that control for confounders are needed to provide a greater degree of certainty in the evidence to inform recommendations.

GUIDELINE LIMITATIONS

The Working Group for this guideline did not include patient representatives. Thus, when developing recommendations, input from patients about their values and preferences was not sought and a systematic review for this information was not performed. Working Group members used their prior clinical experiences with patients with thymic epithelial tumours to assume their relevant values and preferences.

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6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroendocrine and Adrenal Tumors Guideline Version 1.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed [July 28, 2021]. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.