



**PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES**

LUNG SITE

THYMOMA

Lung Site Group – Thymoma

Authors: Dr. Meredith Giuliani, Dr. Andrea Bezjak

1. INTRODUCTION	3
2. PREVENTION	3
3. SCREENING AND EARLY DETECTION	3
4. DIAGNOSIS	3
5. PATHOLOGY	3
6. MANAGEMENT	4
6.1 SURGERY	5
6.2 RADIOTHERAPY	6
6.3 CHEMOTHERAPY	6
6.4 OTHER THERAPY	6
6.4 ONCOLOGY NURSING	7
7. SUPPORTIVE CARE	8
7.1 PATIENT EDUCATION	7
7.2 PSYCHOSOCIAL CARE	7
7.3 SYMPTOM MANAGEMENT	7
7.4 CLINICAL NUTRITION	7
7.5 PALLIATIVE CARE	8

1. INTRODUCTION

Thymoma is a rare thoracic neoplasm which has a long natural history and a tendency to be locally aggressive and recurrent, but rarely metastatic. It is often associated with paraneoplastic syndromes, most commonly myasthenia gravis.

2. PREVENTION

As the etiology of thymoma is unknown there are no prevention strategies.

3. SCREENING AND EARLY DETECTION

The only current form of screening for thymoma is in patients diagnosed with Myasthenia Gravis, who given their high incidence of association with thymic abnormalities (hyperplasia or thymoma) are screened with a thoracic CT at the time of initial diagnosis.

4. DIAGNOSIS

Clinical Evaluation specific to Thymoma:

- Inquire about Myasthenia Gravis (MG) symptoms/signs e.g Diplopia, Ptosis, Slurred speech, Dysphagia, Weakness in Upper or Lower limbs which are fatiguable
- Neurological examination: (Note fatiguable power loss in Myasthenia)

Oncological Imaging:

- CXR, CT chest, occasionally CT abdomen
MRI chest in selected situations, eg to r/o cardiac or vessel involvement

Other Investigations:

- PFTs

5. PATHOLOGY

Thymoma is a thymic epithelial tumor in which the epithelial component exhibits no overt atypia and retains histologic features specific to the normal thymus and contains lymphocytes (which are not malignant) and present in varying numbers. The histologic types of thymoma are defined in the WHO classification. The subtyping is prognostic, with increasingly worse survival with a progression from A through B to C WHO classification. Expert pathology review is beneficial as it may allow more accurate classification of the thymoma subtype.

WHO Classification:

A: Comprised of homogenous population of neoplastic epithelial cells with spindle/oval shape, lacking nuclear atypia, and accompanied by few or no nonneoplastic lymphocytes

AB: Foci with the features of type A thymoma admixed with foci rich in lymphocytes: segregation of two patterns can be sharp or indistinct

B1: Resembles normal functional thymus; combines large expanses with appearance practically indistinguishable from normal thymic cortex with areas resembling thymic medulla

B2: Neoplastic epithelial component appears as scattered plump cells with vesicular nuclei and distinct nucleoli among heavy population of lymphocytes; perivascular spaces are common

B3: Predominantly epithelial cells with round or polygonal shape and exhibiting mild atypia admixed with minor component of lymphocytes; foci of squamous metaplasia and perivascular spaces are common

C: Thymic Carcinoma. A thymic epithelial tumor with cytologic atypia and a set of histologic features no longer specific to the thymus. Lymphocytes that are present are mature and usually admixed with plasma cells

THYMOMA STAGING:

There is currently no TNM staging for thymoma. We utilize the Masaoka Staging system, with Koga modifications. This has also been endorsed internationally (by ITMIG)

- I Grossly and microscopically completely encapsulated tumor
- IIa Microscopic trans-capsular invasion
- IIb Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through mediastinal pleura or pericardium
- III Macroscopic invasion into neighboring organ (i.e. pericardium, great vessel, or lung)
- IVa Pleural or pericardial metastases
- IVb Lymphogenous or hematogenous metastasis

[Ref: Detterbeck FC, et al. The Masaoka-Koga stage classification for thymic malignancies. J Thorac Oncol 2011; 6:S1710-1716.]

6. MANAGEMENT

Thymomas are indolent tumors with a tendency toward local recurrence rather than metastasis. 5-year survival rates range from 50 to 95% depending on the stage and pathological type. However, thymic carcinomas, are typically invasive, and tend to relapse elsewhere with an increased risk of death due to the disease. They present with advanced disease with 5-year survival rates of 30% to 50%. They are often locally advanced, and can be unresectable tumors, or already metastatic and incurable at the time of presentation. The following description applies to management of thymomas (A to B3), not thymic carcinomas:

Stage I - Surgery is mainstay of treatment for stages I-III. Following complete en-bloc surgical excision of a stage I thymoma, there is no benefit to adjuvant radiation therapy of encapsulated noninvasive tumors. Excellent survival that is close to 100%.

Stage II - If pathologically demonstrated capsular invasion, adjuvant radiation therapy following complete surgical excision is not indicated unless there are other worrisome prognostic factors (eg aggressive histological subtype, surgical impression of invasion etc).

Stage III - If resected completely, adjuvant RT has been considered a standard of care. Other options for operable Stage III include Induction chemotherapy followed by surgery with or without RT or Induction chemo-RT followed by surgery.

Operable stage IVA - Options include:

1. Surgical resection with postoperative radiation therapy.
2. Induction chemotherapy followed by surgery with or without RT
3. Induction chemoRT followed by surgery

Inoperable stage III or IV disease:

1. Induction chemotherapy followed by reassessment for a local modality, either surgery or radiation.
2. Induction chemotherapy followed by surgery and radiation.
3. Radiation therapy alone.
4. Chemotherapy alone.

Recurrent disease – considered for aggressive management with intent of disease eradication, including surgery if resectable, +/- RT +/- chemotherapy.

The role of surgical debulking for patients with either stage III or stage IVA disease is controversial and generally not desirable but may be considered on a case-by-case basis.

6.1 Surgery

Mainstay of management is surgery. Complete en-bloc removal of the tumor, entire thymus gland and any involved adjacent structures is typically done through a midline sternotomy or a (inframammary) clamshell or hemi-clamshell incision. The latter is particularly appropriate for large tumours and when excision of pleural deposits is required. Surgery may be a consideration for recurrent disease as well. Special attention needs to be paid to the phrenic nerve, with attempts to preserve it, especially in patients with myasthenia gravis (MG). Patients with MG may present a special perioperative and anaesthetic risk and need to be appropriately managed with respect to their MG by anaesthesia and neurology in the perioperative period.

Resection of pleural deposits (either at time of presentation, or for recurrent disease) is often performed via a thoracotomy. Rarely, pleurectomy may be performed. In exceptional cases, an extrapleural pneumonectomy is considered.

6.2 Chemotherapy

Many chemotherapeutic agents have activity in thymoma. In the concurrent setting, we typically use Cisplatin and Etoposide, in the same doses and timing as for stage III NSCLC. In the setting of neoadjuvant or palliative chemotherapy, cisplatin based regimens are typically used in first line setting.

6.3 Radiation

Radiation is given in several settings:

Postoperatively, in the case of completely resected thymoma, we recommend 40Gy/20 fr for R0, 50Gy/25 fractions for R1 and for incompletely resected tumors (R2), 60 Gy/30 fr. Simulation, planning and delivery of RT follow the principles outlined in the section on planning of lung RT. Volumes are defined on the basis of the OR findings, discussion with the surgeon and any clips left to identify areas of concern about invasion. The original extent of tumor is used as a guide to the appropriate superior-inferior extent of the volume but there is no attempt made to include the entire width of the initial tumor as long as surgical resection was satisfactory in that regard.

Neoadjuvantly, dose of 45Gy/25 fr is delivered concurrently with chemotherapy to the visible tumor with attempts to minimize toxicity to the lung. If the tumor is very bulky and RT field will produce significant risk of lung toxicity, chemotherapy alone followed by surgical resection and postop RT would be the preferred option of management.

For unresectable thymomas, or if a patient is medically inoperable, radical RT alone, to a dose of 66Gy in 33 fr, with or without chemotherapy, would be considered.

For pleural metastases, RT is considered, usually postoperatively, if there is a particular concern about the risk of local recurrence after surgical excision. Volume is defined on the basis of marking clips, and discussion with the surgeon. Doses typically employed are 50Gy/25 fr.

6.4 Other Therapy

Other therapies used in the management of Thymoma include:

High dose rate (HDR) brachytherapy

Used for palliation of endobronchial lesions from thymoma, typically in the setting of previous external beam RT, and typically for palliation - 8Gy single fraction/application.

Interventional Radiology

SVC stent placement for SVCO.

6.5 Oncology Nursing Practice

Refer to [general oncology nursing practices](#)

7. SUPPORTIVE CARE

7.1 Patient Education

Patient education is an integral aspect of cancer management in the lung site group. In addition to one-on-one education specific to the patient situation, there are a multitude of written educational materials that we provide to patients. There are general pamphlets on specific cancers and the main treatments including the Lung Cancer Patient Guide, published by Lung Cancer Canada, 2010. Many from the Canadian Cancer Society, some of which are available in multiple languages, which is useful given the fact that many of our patients do not speak English), as well as specific PMH created brochures that describe specific treatments (eg thoracic radiation, specific chemotherapy regimen etc), specific tests (eg PET scan) and specific symptoms (eg how to manage pain, or fatigue). The specific educational content is provided depending on the patient's diagnosis and management options. In addition, there is a library with resources available to the patient, including books, a Lung Cancer CD-ROM educational Resource and a librarian/patient educator who is available to search for specific information with the patient/family.

7.2 Psychosocial Care

Refer to [general oncology psychosocial care guidelines](#)

7.3 Symptom Management

Lung cancer patients have a multitude of physical and emotional symptoms related to their disease, treatment and co-morbid condition. The common symptoms include pain, dyspnea, fatigue, nausea, vomiting, constipation, anxiety, depression etc. DART and ESAS (Distress Assessment and Response Tool and Edmonton Symptom Assessment System) are the screening tools used to identify the symptoms of most concern to the patient. They add to the clinical assessment of the patient made by the clinician at an individual attendance, but are also recorded serially at each attendance, to observe outcomes of interventions used. Patients answers are reviewed by the nurse and oncologists, symptom management guides are used in response to this screening and patients with significant burden of symptoms can be referred to appropriate services (eg palliative care, social work etc).

7.4 Clinical Nutrition

There is a dedicated dietician for the lung site group. Nutritional advice and support may be required if there has been a substantial weight loss prior to diagnosis, difficulties maintaining oral intake during combined modality treatment (due to esophageal toxicity) or patients with esophageal compression from their malignancy. Occasionally patients

experience dysphasia following surgical interventions which may require nutritional intervention. The goals of nutritional support are to maintain patient's weight throughout treatment and improve any preexisting nutritional deficiencies.

7.5 **Palliative Care**

Refer to [general oncology palliative care guidelines](#)