Provincial Differentiated Thyroid Cancer (DTC) Treatment Guidelines

As per consensus at the Provincial Thyroid Cancer Guideline Meeting
May 26, 2017

Clinical practice guidelines have been developed after multi-disciplinary consensus based on best available literature. As the name suggests, these are to be used as a guide only. These guidelines do not replace physician judgment which is based on multiple factors including, but not limited to, the clinical and social scenario, comorbidities, performance status, age, available resources and funding considerations. The Saskatchewan Cancer Agency disclaims all liability for the use of guidelines except as expressly permitted by the Agency. No portion of these guidelines may be copied, displayed for redistribution to third parties for commercial purposes or any non-permitted use without the prior written permission from the Agency.

Recommendations for drug treatment presented in the Agency's guidelines for a cancer site may not reflect provincial cancer drug funding. Please refer to the current Saskatchewan Cancer Agency drug formulary at www.saskcancer.ca/formulary for information on cancer drug listing and funding.

Benefits and risk of the proposed treatment should be discussed with patient.

Participating in clinical trials is encouraged when available. Involvement of a multidisciplinary team is strongly recommended.

Both nationally and internationally there has been a recognition that, despite a significant increase in the incidence of thyroid cancer worldwide over the past 50 years, there has been no corresponding increase in mortality for this disease. As a corollary, there has been an emerging understanding that a large number of differentiated thyroid cancers have been over treated; an understanding that is reflected in recent clinical practice guidelines. The Saskatchewan Cancer Agency endorses the *2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer* (Haugen, Alexander, *et al.,* Thyroid. Jan 2016, 26(1): 1-133), the key recommendations of which are highlighted below. The major shifts reflected in these guidelines are:

1. A move towards a standardized ultrasound/cytologic concordance system to guide investigation and management of thyroid nodules
2. Acceptance of thyroid lobectomy as an option for many low risk thyroid cancers
3. Acceptance of either no or lower dose radio-iodine treatment for many low risk thyroid cancers
4. Dynamic risk stratified follow-up for thyroid cancer

These paradigm shifts in the investigation and management of thyroid cancer have significantly increased the complexity of decision making for individual patients, a reality that is anticipated to continue into the foreseeable future. Consequently, **the Saskatchewan Cancer Agency highly recommends that patients diagnosed with or suspected to have thyroid cancer be given the opportunity to have their care discussed at the provincial multi-disciplinary cancer rounds held every other week.**

Recommendations:

1. Indications for Surgery
   1.1. Thyroid ultrasound with survey of the cervical lymph nodes should be performed in all patient with known or suspected thyroid nodule.

1.2. Thyroid nodule FNA is recommended based on nodule size and ultrasound characteristics, such as found in the ATA guidelines or the American College of Radiology recommendations (J Am Coll Radiol 2017).
1.3. Thyroid nodule FNA cytology should be reported using diagnostic groups outlined in the Bethesda System for Reporting Thyroid Cytopathology.

2. Risk Classification
2.1. AJCC/UICC staging is recommended for all patients with DTC, based on its utility in predicting disease mortality, and its requirement for cancer registries.
2.2. The 2009 ATA Initial Risk Stratification System is recommended for DTC patients treated with thyroidectomy, based on its utility in predicting risk of disease recurrence and/or persistence.

3. Pre-surgery
3.1. Preoperative neck US for cervical (central and especially lateral neck compartments) lymph nodes is recommended for all patients undergoing thyroidectomy for malignant or suspicious for malignancy cytologic or molecular findings.
3.2. All patients undergoing thyroid surgery should have preoperative voice assessment as part of their pre-operative physical examination. This should include the patient's description of vocal changes, as well as the physician's assessment of voice.

4. Extent of Surgical Resection
4.1. For patients with thyroid cancer >4 cm, or with gross extra-thyroidal extension (clinical T4), or clinically apparent metastatic disease to nodes (clinical N1) or distant sites (clinical M1), the initial surgical procedure should include a near-total or total thyroidectomy and gross removal of all primary tumour unless there are contraindications to this procedure.
4.2. For patients with thyroid cancer >1 cm and <4 cm without extra-thyroidal extension, and without clinical evidence of any lymph node metastases (cN0), the initial surgical procedure can be either a bilateral procedure (near-total or total thyroidectomy) or a unilateral procedure (lobectomy).
4.3. If surgery is chosen for patients with thyroid cancer <1 cm without extra-thyroidal extension and cN0, the initial surgical procedure should be a thyroid lobectomy unless there are clear indications to remove the contralateral lobe.
4.4. Therapeutic central-compartment (level VI) neck dissection **for patients with clinically involved central nodes** should accompany total thyroidectomy to provide clearance of disease from the central neck.
4.5. Therapeutic lateral neck compartmental lymph node dissection should be performed for patients with biopsy-proven metastatic lateral cervical lymphadenopathy.

5. Radioactive Iodine Therapy
5.1. RAI adjuvant therapy should be considered after total thyroidectomy in ATA intermediate risk level differentiated thyroid cancer patients.
5.2. RAI adjuvant therapy is routinely recommended after total thyroidectomy for ATA high risk differentiated thyroid cancer patients.
5.3. If radioactive iodine remnant ablation is performed after total thyroidectomy for ATA low risk thyroid cancer or intermediate risk disease with lower risk features (i.e. low volume central neck nodal metastases with no other known gross residual disease nor any other adverse features), a low administered dose activity of approximately of 30 mCi is generally favored over higher administered dose activities.
5.4. When RAI is intended for initial adjuvant therapy to treat suspected microscopic residual disease, administered activities above those used for remnant ablation up to 150 mCi are generally recommended (in absence of known distant metastases).

6. Follow up
   6.1. Initial recurrence risk estimates should be continually modified during follow-up, because the risk of recurrence and disease specific mortality can change over time as a function of the clinical course of the disease and the response to therapy.
   6.2. Serum Thyroglobulin
      6.2.1. Serum Tg should be measured by an assay that is calibrated against the CRM457 standard. Thyroglobulin antibodies should be quantitatively assessed with every measurement of serum Tg. Ideally, serum Tg and anti-Tg antibodies should be assessed longitudinally **in the same laboratory and using the same assay for a given patient.**
      6.2.2. During initial follow-up, serum Tg on thyroxine therapy should be measured every 6–12 months. More frequent Tg measurements may be appropriate for ATA high-risk patients.
      6.2.3. In ATA low- and intermediate-risk patients that achieve an excellent response to therapy, the utility of subsequent Tg testing is not established. The time interval between serum Tg measurements can be lengthened to at least 12–24 months.
      6.2.4. Serum TSH should be measured at least every 12 months in all patients on thyroid hormone therapy.
      6.2.5. ATA high-risk patients (regardless of response to therapy) and all patients with biochemical incomplete, structural incomplete, or indeterminate response should continue to have Tg measured at least every 6–12 months for several years.
   6.3. Neck Ultrasound
      6.3.1. The first u/s of the thyroid bed and central/lateral nodes should be done at 6-12 months post surgery.
      6.3.2. Follow up u/s should be more frequent when higher risk of recurrence and detectable Tg levels.
      6.3.3. In low risk [after surgery and RAI] without Tg and negative u/s, follow with Tg and examination, **NOT u/s.**
      6.3.4. Suspicious LN>8-10 mm may be followed, but consider FNA if growth or bad location.

Additional resources

American Thyroid Association Cancer Guidelines:
http://online.liebertpub.com/doi/abs/10.1089/thy.2015.0020

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