

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Perioperative Management of Well-Differentiated Thyroid Carcinoma
Evidence-Based Guideline

Definition: Well-differentiated thyroid cancer includes both papillary and follicular thyroid carcinomas.

Epidemiology: The SEER Cancer Statistics reported an incidence of 3.2 per 100,000 for 15-19 year olds, increasing from previous years. ⁽¹⁾ Papillary thyroid carcinoma is the most common malignancy of the thyroid gland in children. ⁽²⁾ Follicular thyroid cancer is uncommon, with medullary thyroid cancer, poorly differentiated tumors, and frankly undifferentiated (anaplastic) thyroid carcinomas are rare in young patients. ⁽³⁾

Inclusion Criteria

- Birth-25 years of age;
- Fine needle aspiration (FNA) biopsy proven well-differentiated thyroid carcinoma (papillary or follicular)
- No clinical or ultrasound evidence of loco-regional metastatic disease

Exclusion Criteria

- >25 year of age, well differentiated thyroid carcinoma with known loco-regional metastatic disease;
- Medullary or anaplastic thyroid carcinoma
- Pregnancy

Diagnostic Evaluation

History: Assess for

- Prior radiation exposure
- Genetic syndromes

Physical Examination

- Visual examination and palpation of the thyroid

Laboratory Tests

- Thyroid function screen (T4 and TSH)
- Thyroglobulin panel
- Thyroid antibodies

Diagnostic Imaging

- Ultrasonography of the thyroid with fine needle aspiration

Surgical Planning

Referral

- Thyroid Tumor Board
- Pediatric surgery or Otolaryngology

Laboratory Tests

- Calcium
- Phosphorous
- Magnesium
- PTH
- Albumin
- Vitamin D 25 Hydroxy

Diagnostic Imaging

- Lymph node mapping if concern for regional disease

Critical Points of Evidence*

Evidence Supports

- To complete initial lymph node mapping with ultrasound pre-operatively to evaluate for regional disease. ⁽⁴⁻¹⁶⁾ – Strong recommendation, low quality evidence
- To evaluate the patient for pre-existing vitamin D deficiency prior to surgery and treat any deficiencies. ⁽¹⁷⁻²⁴⁾ – Strong recommendation, very low quality evidence
- To check postoperative parathyroid hormone and calcium levels to evaluate for hypoparathyroidism and hypocalcemia. ⁽²⁵⁻²⁷⁾ – Strong recommendation, low quality evidence
- To administer post-operative oral calcium supplementation to patients post-thyroidectomy to avoid transient hypocalcemia. ⁽²⁸⁻³⁰⁾ – Strong recommendation, moderate quality evidence

Evidence Against

- The routine use of computed tomography to evaluate for regional disease for pre-thyroidectomy evaluation. ⁽⁴⁻¹⁶⁾ – Strong recommendation, low quality evidence
- Prophylactic central neck dissection in patients with papillary thyroid carcinoma and no loco-regional metastases. ⁽³¹⁻³⁹⁾ – Strong recommendation, moderate quality evidence
- The use of pre-operative calcium supplementation. ^(30,40) – Strong recommendation, very low quality evidence

Evidence Lacking/Inconclusive

- The use of intermittent recurrent nerve monitoring during surgery to reduce incidence of nerve injury. ⁽⁴¹⁾ – Unable to make a recommendation

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

Admission Criteria

- Admit for post-thyroidectomy care

Discharge Criteria

Patient can go home on calcium carbonate BID and calcitriol daily on postop if the patient has no hypocalcemia symptoms, no calcium level <8.5 during hospitalization, and an intra-op PTH >30.

Consults/Referrals

Endocrinology to follow and order weekly labs to wean calcium and calcitriol supplementation and manage thyroid hormone replacement therapy.

Follow-Up Care

- Thyroid replacement: Liothyronine
 - Age <10 years: 25 mcg daily
 - Age ≥10 years: 50 mcg daily

Parent/Caregiver Teaching

- Signs and symptoms of hypocalcemia: perioral and acral paresthesias, stiffness, clumsiness, myalgias, muscle spasms, diaphoresis, seizures.

Measures

Process

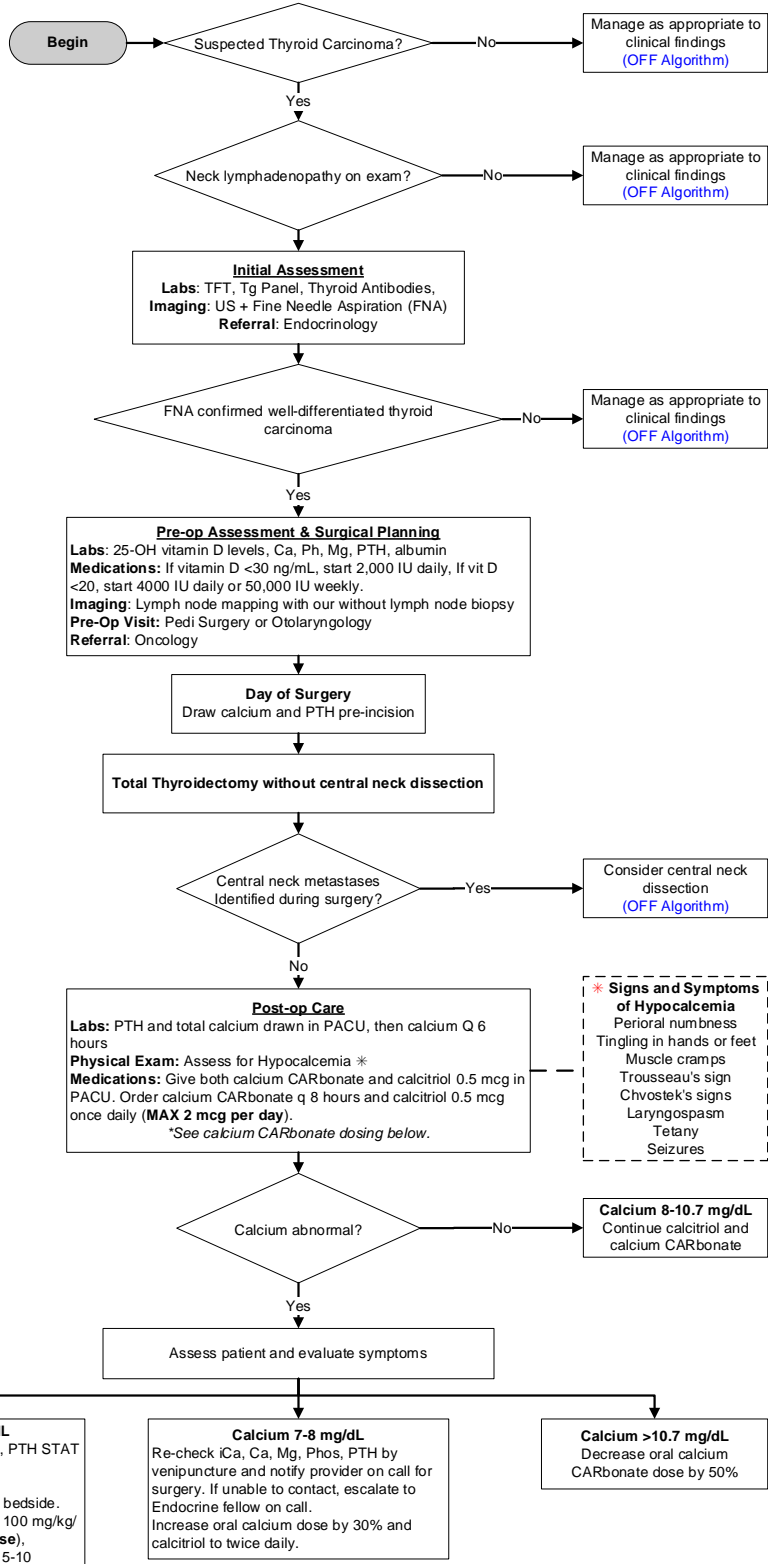
- Central and lateral neck dissections
- Use of recurrent nerve monitoring
- Post-operative laryngoscopy
- Readmissions or emergency center visits
- Returns to OR

Outcome

- Post-op transient hypocalcemia during hospitalization
- Rates of IV calcium use during hospitalization
- Patients requiring calcium supplementation at 6 months and 1 year post-op
- Recurrent laryngeal nerve injury

**Texas Children's Hospital Evidence-Based Outcomes Center
Perioperative Management of Well-Differentiated Thyroid Carcinoma Algorithm**

- Exclusion Criteria**
- >25 year of age
 - well differentiated thyroid carcinoma with known loco-regional metastatic disease
 - medullary or anaplastic thyroid carcinoma
 - pregnancy.



- * Signs and Symptoms of Hypocalcemia**
- Perioral numbness
 - Tingling in hands or feet
 - Muscle cramps
 - Trousseau's sign
 - Chvostek's sign
 - Laryngospasm
 - Tetany
 - Seizures

Post-operative Calcium CARbonate Dosing

Weight	Calcium CARbonate Dose
10-20 kg	250 mg
21-40 kg	750 mg
41-49 kg	1,000 mg
>50 kg	1,500 mg

Available Preparations: Suspension 250 mg/mL; Tablet 500 mg

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children’s Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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Clinical standard developed through the Evidence Based Outcomes Center (EBOC).

No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
 - PICO questions established
 - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
 - NCCN Guidelines: Thyroid Carcinoma by the National Comprehensive Cancer Network (2016)
 - Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer by the American Thyroid Association Guidelines Task Force on Pediatric Thyroid Cancer (2015)
 - Guidelines for the Management of Thyroid Cancer by the British Thyroid Association (2014)
 - Clinical Practice Guideline: Improving Voice Outcomes after Thyroid Surgery by the American Academy of Otolaryngology—Head and Neck Surgery (2013)
 - Thyroid Carcinoma by the American College of Radiology (2013)
 - Thyroid Cancer: EMSO Clinical Practice Guidelines for Diagnosis, Treatment, and Follow-Up by the European Society for Medical Oncology (2012).
3. Literature Review of Relevant Evidence
 - Searched: PubMed, Cochrane, AHRQ, National Institute for Clinical Excellence, Google Scholar

4. Critically Analyze the Evidence
 - Nine of meta-analyses, two randomized controlled trials, and twenty-seven nonrandomized studies.
5. Summarize the Evidence
 - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Perioperative Management of Well-Differentiated Thyroid Carcinoma evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline. This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions. **“Evidence Supports”** provides evidence to support an intervention. **“Evidence Against”** provides evidence against an intervention. **“Evidence Lacking/Inconclusive”** indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*. The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the management of well-differentiated thyroid carcinoma in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner should use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

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Version History

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April 2018	Originally Completed	
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