Ultrasound for Pre-operative Evaluation of Well Differentiated Thyroid Cancer

Its Not Just About the Nodes

AACE Advances in Medical and Surgical Management of Thyroid Cancer - 2017

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Objectives

- Discuss the impact of the pre-operative ultrasound on surgical planning.
  - Lymph nodes
  - Additional factors in risk stratification.
- Review features of benign and malignant lymph nodes.
- Review findings on pre-operative ultrasound associated with high risk of recurrence.
- Critically analyze the 2015 ATA Guidelines regarding biopsy of suspicious lymph nodes.
Differentiated Thyroid Cancer

- 62,500 New cases of DTC in 2015
  - Doubled over last decade
  - Tripled over last two decades.

- 1,950 Deaths - Stable
  - Mortality not significantly changed over past 30 years

Assumption: Early detection and treatment of cervical metastases will affect mortality
- Mortality versus Morbidity
Cervical Lymph Nodes

• Approximately 300 lymph nodes in the normal neck.
• Typically can identify 6 – 20 nodes by ultrasound.
• Nodes are more prominent following infections, mononucleosis, dental procedures and in Hashimoto’s thyroiditis.
Preoperative Imaging

- WDTC clinically involves lymph nodes in approximately 15 - 20% of patients and in most cases can be detected on ultrasound.
- Micrometastases are present in up to 90%.
- Surgical management is altered in the presence of clinical lateral neck metastases.
  - Total Thyroidectomy
  - Central Neck Dissection! (ATA Guidelines 2015)
  - Lateral Neck Dissection

Kouvaraki, Surgery 2003 134:946; Stulak, Arch Surg 2006 141:489
Fig 8. Influence of nodal status at initial operation on cumulative risk of recurrence (any site). Graphs are based on 892 patients without initial distant metastases and with complete tumor resection.
ATA Risk of Recurrence - Stratification Based on Initial Staging - 2009

- **LOW RISK**
  - Classic PTC / WDTC
  - Complete resection
  - No Extra-thyroidal extension.
  - No vascular invasion

- **INTERMEDIATE RISK**
  - Microscopic Extra-thyroidal extension
  - Cervical Lymph node Mets
  - Aggressive Histology
  - Vascular invasion

- **HIGH RISK**
  - Macroscopic gross Extra-thyroidal extension
  - Incomplete tumor resection
  - Thyroglobulin elevation
  - Distant Mets
Risk of Structural Disease Recurrence
(In patients without structurally identifiable disease after initial therapy)

Modified 2009 Risks

High Risk
Gross extrathyroidal extension, incomplete tumor resection, distant metastases, or lymph node >3 cm

Intermediate Risk
Aggressive histology, minor extrathyroidal extension, vascular invasion, or > 5 involved lymph nodes (0.2-3 cm)

Low Risk
Intrathyroidal DTC ≤ 5 LN micrometastases (< 0.2 cm)

FTC, extensive vascular invasion (≈ 30-55%)
pT4a gross ETE (≈ 30-40%)
pN1 with extranodal extension, >3 LN involved (≈ 40%)
PTC, > 1 cm, TERT mutated ± BRAF mutated* (>40%)
pN1, any LN > 3 cm (≈ 30%)
PTC, extrathyroidal, BRAF mutated*(≈ 10-40%)
PTC, vascular invasion (≈ 15-30%)
Clinical N1 (≈20%)
pN1, > 5 LN involved (≈20%)
Intrathyroidal PTC, < 4 cm, BRAF mutated* (≈10%)
pT3 minor ETE (≈ 3-8%)
pN1, all LN < 0.2 cm (≈5%)
pN1, ≤ 5 LN involved (≈5%)
Intrathyroidal PTC, 2-4 cm (≈ 5%)
Multifocal PMC (≈ 4-6%)
pN1 with extranodal extension, ≤ 3 LN involved (2%)
Minimally invasive FTC (≈ 2-3%)
Intrathyroidal, < 4 cm, BRAF wild type* (≈ 1-2%)
Intrathyroidal unifocal PMC, BRAF mutated*, (≈ 1-2%)
Intrathyroidal, encapsulated, FV-PTC (≈ 1-2%)
Unifocal PMC (≈ 1-2%)

*While analysis of BRAF and or TERT status is not routinely recommended for initial risk stratification, we have included these findings to assist clinicians in proper risk stratification in cases where this information is available.
Pre-operative Comprehensive Neck Ultrasound

- The pre-operative neck US is for more than just cervical lymph nodes.
  - Evaluate thyroid for signs indicative of high risk of aggressive disease
    - Size of primary tumor.
    - Suggestion of multifocality.
    - Location of cancer (Adjacent to trachea or recurrent laryngeal nerve).
    - Suspicion of extrathyroidal extension.
17 patients underwent reoperation for thyroid cancer at MD Anderson less than 6 months after initial surgery. Pre-operative Ultrasound would likely have prevented 70% or the repeat operations.
Clinical (PE) Lymph Node (LN) Metastases at Presentation: WORSE Outcome

![Graph showing local and nodal recurrence rates](Image)

- Local Recurrence
  - LN positive
  - LN negative

- Nodal Recurrence
  - LN positive
  - LN negative

Reurrence (%) vs Years after initial surgery

- Local Recurrence: LN positive vs LN negative
- Nodal Recurrence: LN positive vs LN negative

Statistical significance:
- Local Recurrence: p<0.001
- Nodal Recurrence: p<0.001

Hay, Surgery 1992
US Detects about 40% of Pathologically Abnormal LNs

US (-), PATHOLOGY (+) LN Metastases: NO IMPACT on Outcome

Ito, Word J Surg 2004

p=NS
Does lateral neck dissection alteration the outcome for patients with preoperative ultrasound positive for lymph nodes?

Prophylactic lateral neck dissection does NOT improve recurrence free survival for patients with preoperative ultrasound negative for lymph nodes\(^1\)

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\(^1\) Ito, World J Surg 2004
For macroscopic lateral lymph node metastases, modified neck dissection at time of initial thyroidectomy improves survival.
RECOMMENDATION 6

Thyroid sonography with survey of the cervical lymph nodes should be performed in all patients with known or suspected thyroid nodules. *(Strong recommendation, High-quality evidence)*

Sonographic evaluation of the anterior cervical lymph node compartments (central and lateral) should be performed whenever thyroid nodules are detected. If ultrasound detects cervical lymph nodes that are sonographically suspicious for thyroid cancer (Table 8), FNA of the suspicious lymph node should be performed for cytology and washout for thyroglobulin measurement if indicated. In addition, this scenario also warrants US-guided FNA of a subcentimeter nodule that is likely to represent the primary tumor based upon sonographic features.
RECOMMENDATION 32

A) 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. (Strong recommendation, Moderate-quality evidence)

B) US-guided FNA of sonographically suspicious lymph nodes $> 8-10$ mm in the smallest diameter should be performed to confirm malignancy if this would change management. (Strong recommendation, Moderate-quality evidence)

C) The addition of FNA-Tg washout in the evaluation of suspicious cervical lymph nodes is appropriate in select patients, but interpretation may be difficult in patients with an intact thyroid gland. (Weak recommendation, Low-quality evidence)
Characteristics of Benign Lymph Nodes

- Flattened or oval shape
  - Short / long axis < 0.5
- Echogenic (hilar) line
- Vascular flow limited to hilum on Doppler
- Size varies with compartment and is less important than morphology.
- Border characteristics are also less important.
The Hilar Line

- A normal node can be split down the central hilum.
- Hilum contains fat and vessels
- A normal hilar line can be thin or thick, and can be central or eccentric/diagonal.
- The presence of a hilar line is reassuring, but it’s absence in not considered suspicious.
Characteristics of Metastatic Lymph Nodes

- Calcifications
- Cystic necrosis
- Chaotic (peripheral) vascularization
- Rounded appearance
  - Short/Long Axis > 0.5
- Jugular displacement
- Absent echogenic (hilar) line
Table 8: Ultrasound features of lymph nodes predictive of malignant involvement. (adapted with permission from the European Thyroid Association guidelines for cervical ultrasound (20))

<table>
<thead>
<tr>
<th>Sign</th>
<th>Reported sensitivity %</th>
<th>Reported specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcalcifications</td>
<td>5-69</td>
<td>93-100</td>
</tr>
<tr>
<td>Cystic aspect</td>
<td>10-34</td>
<td>91-100</td>
</tr>
<tr>
<td>Peripheral vascularity</td>
<td>40-86</td>
<td>57-93</td>
</tr>
<tr>
<td>Hyperechogenicity</td>
<td>30-87</td>
<td>43-95</td>
</tr>
<tr>
<td>Round shape</td>
<td>37</td>
<td>70</td>
</tr>
</tbody>
</table>
A correlation performed between US findings and pathology at surgery (292) has shown for lymph nodes > 7 mm in the smallest diameter, that a cystic appearance or hyperechoic punctuations in a context of thyroid cancer should be considered as malignant; lymph nodes with a hyperechoic hilum are reassuring; the type of vascularization (central: reassuring; peripheral: concerning) has a high sensitivity/ specificity; a round shape, a hypoechoic appearance or the loss of the hyperechoic hilum by themselves does not justify a FNAB.

Interpretation of neck US should take into account all other clinical and biological data.
Disordered (peripheral) vascularity
Size > 3cm is associated with high risk of Recurrent disease
Jugular Displacement
Papillary Carcinoma – Tall Cell – Calcified Node
Papillary Carcinoma – Node – Chaotic Vascularity
Pre-operatively, central compartment lymph nodes are often much more difficult to visualize than lateral nodes, but should be investigated.
Investigation of the central compartment includes inferior to the thyroid.
Prognostic Indicators for Recurrence
Nodal factors

- Lymph node metastases larger than 3 cm
- Extra-nodal extension
- More than 5 lymph nodes involved
- Aggressive Subtype (Tall Cell, TERT)
- High ratio of positive/removed nodes
RECOMMENDATION 32

A) 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. (Strong recommendation, Moderate-quality evidence)

B) US-guided FNA of sonographically suspicious lymph nodes > 8-10 mm in the smallest diameter should be performed to confirm malignancy if this would change management. (Strong recommendation, Moderate-quality evidence)

C) The addition of FNA-Tg washout in the evaluation of suspicious cervical lymph nodes is appropriate in select patients, but interpretation may be difficult in patients with an intact thyroid gland. (Weak recommendation, Low-quality evidence)
Should this solitary <0.7 cm metastatic node undergo biopsy prior to thyroidectomy?
Should this solitary 0.6 cm atypical node undergo biopsy prior to thyroidectomy?
The pre-operative neck US assesses more than just cervical lymph nodes.

- Evaluate the thyroid for signs indicative of high risk of aggressive disease
  - Size of index thyroid lesion.
  - Multifocality.
  - Suspicion of extrathyroidal extension.
  - Location of cancer
    - Adjacent to trachea or RLN
    - Isthmus lesions have higher rate of ETE
Preoperative Factors Associated with Higher Risk of Recurrence

- **Lesion factors**
  - Extrathyroidal Extension (ETE)
  - Location (Adjacent to RLN or trachea)
  - Nodes - Number and size (ENE)
  - Percent of tumor abutting thyroid capsule

- **Signs or symptoms of invasion of RLN or trachea**

- **FNAB findings of high grade malignancy**

- **Patient factors**
  - Familial cancer, radiation
Extra-thyroidal extension is difficult to detect

- 79 Thyroid cancers evaluated for ETE on pre-op ultrasound, both 2D and 3D.
- Mean size 1 cm
  - 71% < 1 cm
- 52/79 (66%) showed extra-thyroidal extension.
  - ETE $\rightarrow$ pT3 or pT4
- Accuracy for predicting ETE 61%
  - Increased to 68% if combined with 3D US

Extrathyroidal Extension into Strap Muscles
Suspicious for Extrathyroidal Extension
Suspicious for Extrathyroidal Extension
Extensive abutment of thyroid capsule suggests a high risk for ETE

Pre-operative Ultrasound Conclusions

- A comprehensive central / lateral preoperative ultrasound should be performed in all patients undergoing surgery for thyroid cancer.
- Risk stratification should aid in planning the extent of thyroid surgery, as well as the need for a high volume thyroid surgeon.
- Consider biopsy of ANY suspicious nodes.
- Additional factors including: size, location, extrathyroidal extension and abutment ratio should be considered in surgical planning.
- Provide a detailed pre-operative map.