Managing thyroid disease, NICE guidelines and thyroid nodules/goitre

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Overview

- Managing thyroid disease: an endocrinologist perspective
- Goitre and nodules
- What’s new in the NICE guidelines

NICE Thyroid Diseases Guidelines 2019 [https://www.nice.org.uk/guidance/ng145](https://www.nice.org.uk/guidance/ng145)
Vasileiou et al. BMJ 2020 368:m41
Thyroid gland anatomy

- Located in neck
- Brownish-red
- 25-30 g
- Thin fibrous capsule of connective tissue
- Right and left lobes united by a narrow isthmus
Cell types in the thyroid gland

- Follicular cell
- Thyroid epithelial / Follicular cell
- C-cell
- Basement membrane
- Capillary
- Lymphatic vessel
- Colloid
- Sympathetic nerve ending
Thyroid hormones

- Control of metabolism: energy generation and use
- Regulation of growth
- Multiple roles in development
Thyroid hormones

T3: Triiodothyronine

\[
\begin{align*}
  &\text{HO} \quad \text{O} \quad \text{O} \quad \text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}
  \\
  &\text{I} \quad \text{I} \quad \text{I}
\end{align*}
\]

T4: Thyroxine

\[
\begin{align*}
  &\text{HO} \quad \text{O} \quad \text{O} \quad \text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}
  \\
  &\text{I} \quad \text{I}
\end{align*}
\]
Thyroid hormones

- T3 is biologically active hormone
- Produced by mono-deiodination of T4 which is most abundant
- Deiodinase (D1, D2, D3) enzymes present in peripheral tissues
Thyroid hormone binding proteins

TBG: Thyroxine binding globulin

Free T4: 0.03%
Free T3: 0.3%
Tests of thyroid function

- Serum TSH
- Serum free T4
- Serum free T3

Hyperthyroidism:
- ↓ Serum TSH
- ↑ Serum free T4
- ↑ Serum free T3

Hypothyroidism:
- ↑ Serum TSH
- ↓ Serum free T4
- ↓ Serum free T3
## Prevalence of thyroid disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>- prevalence:</th>
<th>- incidence:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td>2.7%</td>
<td>0.1%/yr (♀ &gt; ♂)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>5%</td>
<td>0.4%/yr (♀ &gt; ♂)</td>
</tr>
<tr>
<td>Goitre</td>
<td>24.4%</td>
<td>0.2% (♀ &gt; ♂)</td>
</tr>
</tbody>
</table>

Information to patients, carers and families

- Thyroid disease usually responds well to treatment
- Goal: alleviate symptoms and align TFT to normal/close to normal
- Potential discrepancy between symptoms and tests
- Provide info on condition, treatment, risks of treatment, when to seek advice
- Sections on hypo-, hyperthyroidism and enlargement

NICE Thyroid Diseases Guidelines 2019 https://www.nice.org.uk/guidance/ng145
Thyroid enlargement
Definition: “Discrete lesions within the thyroid gland, radiologically distinct from surrounding parenchyma”

- May be discovered on palpation, imaging, incidentally
- Most common in women (4:1) and in older populations
- Increased in areas of low iodine intake

Cooper DS et al. 2009 Revised ATA Guidelines Thyroid 2009, 19: 1167-1214
Significance of thyroid nodules

- May cause thyroid dysfunction
- May cause compression
- Need to exclude thyroid cancer

- Prevalence of malignancy is 4 – 6.5%
- Independent of nodule size
- Malignancy risk in incidentalomas remains controversial
- Risk of PET-positive thyroid nodule: 27%
UK Thyroid Cancer Incidence

- < 1% of all cancers
- Incidence in UK = 3.2 per 100,000
- Male:female = 1:3 (1:13 in Japan)
- 2013: 3,241 new cases – 373 deaths

Cancer Research UK, 2013
Thyroid ultrasound
### Features suggestive of malignancy

<table>
<thead>
<tr>
<th>History</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Hx of MEN, MTC, PTC</td>
</tr>
<tr>
<td>History of head and neck irradiation</td>
</tr>
<tr>
<td>History of Hodgkin and non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>Age &lt; 20</td>
</tr>
<tr>
<td>Age &gt; 70</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Symptoms of compression: hoarseness, dysphagia, dyspnoea, cough, dysphonia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firm nodule</td>
</tr>
<tr>
<td>Nodule fixed to adjacent structures</td>
</tr>
<tr>
<td>Growth of nodules, especially during therapy to suppress TSH</td>
</tr>
<tr>
<td>Abnormal cervical lymph nodes</td>
</tr>
<tr>
<td>Vocal cord paralysis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspicious US features</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
</tr>
</tbody>
</table>

*Hegedus 2004 NEJM;351:1764-1771*
 Thyroid ultrasonography

- Extremely sensitive for diagnosis of thyroid nodules
- Specific for thyroid ca diagnosis (papillary)
- Aids decision making to select nodules for FNA
- Increases yield of diagnostic FNA
- Patients with possible thyroid cancer should undergo ultrasonographic evaluation of neck by experienced operator

British Thyroid Association, RCP 2014 Revised guidelines for the management of thyroid cancer

Clin Endo (2014) 81: 1-122
<table>
<thead>
<tr>
<th>Benign nodule</th>
<th>Malignant nodule: Papillary/medullary</th>
<th>Follicular lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spongiform/honeycomb</td>
<td>Solid and hypoechoic</td>
<td>Hyperechoic/homogeneous/halo benign</td>
</tr>
<tr>
<td>Purely cystic</td>
<td>Irregular margin</td>
<td>Hypoechoigency/loss of halo suspicious</td>
</tr>
<tr>
<td>Egg shell calcification</td>
<td>Intranodular vascularity</td>
<td></td>
</tr>
<tr>
<td>Iso/hyper echoic (hypoechoic halo)</td>
<td>Absence of halo</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascularity</td>
<td>Taller than wide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microcalcifications</td>
<td></td>
</tr>
</tbody>
</table>
Scoring system: U1-U5

U1: Normal
U2: Benign
U3: Indeterminate
U4: Suspicious
U5: Malignant

British Thyroid Association, RCP 2014 Revised guidelines for the management of thyroid cancer
Clin Endo (2014) 81: 1-122
<table>
<thead>
<tr>
<th>Classification</th>
<th>Cytology</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thy 1</td>
<td>Non-diagnostic</td>
<td>US +/- repeat FNA</td>
</tr>
<tr>
<td>Thy 2</td>
<td>Non-neoplastic</td>
<td>Correlate with clinical and US findings</td>
</tr>
<tr>
<td>Thy 3a</td>
<td>Neoplasm possible (atypical features)</td>
<td>Further US +/- FNA MDT discussion if Thy3a on repeat sample</td>
</tr>
<tr>
<td>Thy 3f</td>
<td>Follicular neoplasm</td>
<td>Diagnostic hemi-thyroidectomy</td>
</tr>
<tr>
<td>Thy 4</td>
<td>Suspicious of malignancy</td>
<td>Diagnostic hemi-thyroidectomy</td>
</tr>
<tr>
<td>Thy 5</td>
<td>Diagnostic of malignancy</td>
<td>Therapy appropriate to tumour type: usually surgery</td>
</tr>
</tbody>
</table>

*British Thyroid Association, RCP 2014 Revised guidelines for the management of thyroid cancer Clin Endo (2014) 81: 1-122*
Investigation of thyroid enlargement (nl TFT)

- US in palpable enlargement or nodule if malignancy suspected
- Consider US in incidental nodules if malignancy possible
- Use grading system to decide on FNA taking into account:
  - Echogenicity
  - Microcalcifications
  - Border
  - Shape in transverse plane
  - Internal vascularity
  - Lymphadenopathy

NICE Thyroid Diseases Guidelines 2019 https://www.nice.org.uk/guidance/ng145
Investigation of thyroid enlargement (nl TFT)

- US reports should
  - Include information on the features AND
  - provide an overall assessment of malignancy, AND
  - specify which grading system has been used

- Use US for FNA

*NICE Thyroid Diseases Guidelines 2019 [https://www.nice.org.uk/guidance/ng145](https://www.nice.org.uk/guidance/ng145)*
Managing thyroid enlargement

- Don’t offer treatment if mild/no symptoms unless:
  - Breathing difficulty
  - Clinical concern (airway narrowing)

- Repeat US and TSH if
  - Symptoms worsen OR
  - New symptoms develop (hoarseness, SOB) OR
  - Malignancy suspected OR
  - Compression suspected

*NICE Thyroid Diseases Guidelines 2019* [https://www.nice.org.uk/guidance/ng145](https://www.nice.org.uk/guidance/ng145)
Managing thyroid enlargement

- Cyst/predominantly cystic lesion offer aspiration
- Possible ethanol ablation if re-accumulation
- Non-cystic non malignant nodule with symptoms
  - Surgery (if airway narrowing)
  - RAI if demonstrable iodine uptake
  - Percutaneous thermal ablation

NICE Thyroid Diseases Guidelines 2019 https://www.nice.org.uk/guidance/ng145
Highlights of NICE guidelines

- Importance of information
- Less TFT testing in T2DM
- Cascading system of testing
- No repeat testing of TPO
- Liothyronine should not be routinely prescribed for overt hypothyroidism
- Treatment of SC hypo in < 65 of TSH > 10
- 6 month trial if TSH < 10 and symptoms

NICE Thyroid Diseases Guidelines 2019 https://www.nice.org.uk/guidance/ng145
Highlights of NICE guidelines

- Diagnose aetiology of hyperthyroidism (TRAB, Tc)
- Radioiodine as first line treatment for Graves’ and TN hyperthyroidism
- Consider treatment of SC Hyper if TSH < 0.1 mIU/L
- US and FNA for thyroid enlargement
- No treatment or repeat scanning of benign thyroid enlargement with normal thyroid function unless indicated

NICE Thyroid Diseases Guidelines 2019 https://www.nice.org.uk/guidance/ng145