The Evaluation of the Utility of Calcitonin as a Screening Tool for Medullary Thyroid Carcinoma in Patients with Nodular Thyroid Disease

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Introduction:
• The use of serum calcitonin to screen patients with nodular thyroid disease remains controversial due to conflicting data regarding its sensitivity, specificity and cost effectiveness in detecting medullary thyroid cancer (MTC).
• Currently, the routine use of calcitonin is recommended by the European consensus group but not the American or British Thyroid Associations. 1-3

Aims:
• To formally evaluate the utility of calcitonin as a screening tool for MTC in patients presenting with nodular thyroid disease to outpatient services at a tertiary endocrine centre.

Methods:
• Retrospective study of all adult patients undertaking calcitonin measurement during their first presentation to an outpatient thyroid nodule clinic in a single centre (n=302).
• Exclusion criterion: patients in whom calcitonin levels were measured in non-thyroid settings. Patients with previously documented MTC, MEN or positive RET mutation and patients with insufficient data.
• Data from eligible patients were obtained from their electronic patient records (EPR).
• A direct, two-site, sandwich type chemiluminescence immunoassay (CLIA, Diasorin, Berkshire, United Kingdom) was used for quantitative determination of calcitonin.
• The minimum detectable dose is 1.0ng/L. Calcitonin was deemed elevated if ≥4.8ng/mL for females and ≥11.8ng/mL for males.

Results:
• 20/302 (6.6%) patients had calcitonin measurement above the sex-dependent threshold and 2 (0.7%) had a raised CEA. [Fig. 1.]
• FNAC performed in 178/302 (58.9%) of patients:
  • Thy1: 15.7%
  • Thy1c: 6.2%
  • Thy2: 57.3%
  • Thy3: 18.0%
  • Thy4: 1.1%
  • Thy5: 1.7%
• Final histological evidence was available in 86/302 (28.5%) of cases.

Table 1: Baseline characteristics of the study population.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Sample (n=302)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(±15.7)</td>
</tr>
<tr>
<td>Sex</td>
<td>F = 84.1%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Caucasian:</td>
<td>40.1%</td>
</tr>
<tr>
<td>Afro-Caribbean:</td>
<td>29.7%</td>
</tr>
<tr>
<td>Asian:</td>
<td>5.6%</td>
</tr>
<tr>
<td>Other:</td>
<td>7.0%</td>
</tr>
<tr>
<td>Not Stated:</td>
<td>17.5%</td>
</tr>
</tbody>
</table>

![Figure 1: Schematic representation of the outcome of raised calcitonin](image)

Conclusions:
• Current literature: In patients referred for evaluation of thyroid nodular disease, 10-40% with an elevated calcitonin were associated with a new diagnosis of MTC.4
• Our study: 20/302 (6.6%) patients had an elevated calcitonin and 2/20 (10%) of these were associated with a new diagnosis of MTC
• Both cases of MTC had abnormal radiological and cytological findings.
• Calcitonin screening did not identify any cases of MTC with otherwise normal or indeterminate parameters.
• Although case numbers were low, calcitonin did not appear to provide added value as a screening tool for MTC in thyroid nodular disease.

References:
1. The European Thyroid Cancer Taskforce. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. European Journal of Endocrinology 2006; 154: 787–803