**Prediction of lymph node metastasis in papillary thyroid cancer by preoperative BRAF analysis, Is it useful?**

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**Introduction and Aim**

Prophylactic central lymph node dissection (CLND) in patients with suspected papillary thyroid cancer (PTC) without evident lymph node metastasis (LNM), remains debatable. We propose to evaluate whether BRAF V600E mutation presence, could help to identify patients at risk for LNM.

**Methods**

Retrospective study of patients with diagnosis of differentiated thyroid cancer, who underwent total thyroidectomy during 2002 and 2013 (n:256) in our hospital. Patients with pathological diagnosis of PTC, whose BRAF V600E mutation status was known (n:170) and who underwent lymphadenectomy (n:118) as well, were selected. LNM presence was correlated with BRAF V600E mutation status (presence of BRAF V600E mutation vs wild type) and with other clinico-pathological factors (age, initial tumor size, gender, etc).

A multivariate analysis was performed to assess independent factors related to LNM.

DNA was extracted from paraffin-embbebed tissues section and V600E mutations were detected by HRM followed by sequencing confirmation.

**Results**

**Table 1: Demographic and pathological characteristics of the cohort**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>YES</th>
<th>NO</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: female / male</td>
<td>88 (74.6%) / 30 (25.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>44.8 ±15.5 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time from diagnosis (months)</td>
<td>42.0 ± 29.1 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classical PTC (n, %)</td>
<td>86 (72.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph node metastasis (n, %)</td>
<td>71 (60.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrathyroidal invasion (n, %)</td>
<td>43 (36.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant metastasis (n,%)</td>
<td>6 (6,6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AJCC stage (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>66 (55.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>12 (10.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>13 (11.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV a</td>
<td>18 (15.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV c</td>
<td>3 (2.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (5,1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Data expressed as median ± sd

**Table 2: Characteristics associated with LNM**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LNM YES</th>
<th>LNM NO</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 45 years</td>
<td>52.0%</td>
<td>48%</td>
<td>0.120</td>
</tr>
<tr>
<td>Male Sex</td>
<td>76.7%</td>
<td>23.3%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Size &gt; 1 cm</td>
<td>59.5%</td>
<td>40.5%</td>
<td>0.914</td>
</tr>
<tr>
<td>Size &gt; 2 cm</td>
<td>66.7%</td>
<td>33.3%</td>
<td>0.233</td>
</tr>
<tr>
<td>Extrathyroidal invasion</td>
<td>74.4%</td>
<td>25.6%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Multifocality</td>
<td>42.6%</td>
<td>57.4%</td>
<td>0.187</td>
</tr>
</tbody>
</table>

**Table 3 Multivariate analysis: Variables independently associated with the presence LNM**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR</th>
<th>CI 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrathyroidal invasion</td>
<td>3.0</td>
<td>1.8-7.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.35</td>
<td>0.12-1.04</td>
<td>0.057</td>
</tr>
<tr>
<td>Age &gt; 45 years</td>
<td>2.23</td>
<td>0.92-5.3</td>
<td>0.073</td>
</tr>
<tr>
<td>BRAF V600E</td>
<td>0.61</td>
<td>0.25-1.46</td>
<td>0.269</td>
</tr>
<tr>
<td>Size &lt; 2 cm</td>
<td>0.74</td>
<td>0.31-1.81</td>
<td>0.515</td>
</tr>
<tr>
<td>Multifocality</td>
<td>1.2</td>
<td>0.52-3.01</td>
<td>0.616</td>
</tr>
</tbody>
</table>

**Conclusions**

Our results do not support using the presence of V600E mutation to decide whether to perform or not prophylactic CLND in patients with PTC. More prospective studies will be necessary.