Cardiovascular Risk Factors in Autoimmune Thyroiditis and Subclinical Hypothyroidism

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Introduction
• Subclinical hypothyroidism (SCH) is defined by high seric levels of TSH and normal levels of free T3 (FT3) and free T4 (FT4). Nearly 60-80% of cases with SCH are associated with Hashimoto thyroiditis.
• There is increasing evidence that subclinical hypothyroidism (SCH) is related with an increased cardiovascular risk. Some studies have reported high levels of total cholesterol and LDL-cholesterol and low levels of HDL-cholesterol in patients with SCH. It has also been reported an association between SCH, insulin resistance and low grade systemic inflammation.

Objective
To evaluate the relationship between autoimmune thyroiditis, subclinical hypothyroidism and cardiovascular risk factors.

Methods
• We assessed medical records of 255 patients with autoimmune thyroiditis from the consultation of Endocrinology from our institution.
• Patients with other autoimmune diseases, diabetes mellitus, oncologic pathology, previous cardiovascular events and taking medication to dyslipidemia or thyroid disease were excluded.
• We defined 2 groups:
  • Group 1 (n = 69) – euthyroid state: TSH 0.35-2.5 μIU/ml, FT3 1.71 - 3.71 pg/ml and FT4 0.70-1.48 ng/dl
  • Group 2 (n = 186) – subclinical hypothyroidism: TSH> 2.5 μIU/ml, FT3 1.71 - 3.71 pg/ml and FT4 0.70 - 1.48 ng/dl
• We recorded thyroid function tests, anti-TPO and anti-thyroglobulin antibodies, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, apolipoprotein A1, apolipoprotein B, lipoprotein(a), homocysteine, high sensitivity CRP, folic acid, vitamin B12, HOMA-IR (Homeostasis model assessment insulin resistance), HOMA-B (Homeostasis model assessment β cell), QUICKI (Quantitative insulin sensitivity check index), HSI (Hepatic insulin sensitivity index), WBISI (Whole body insulin sensitivity index) and IGI (Insulogenic Index) for both groups.
• Statistical analysis was performed with Mann-Whitney test, logistic regression and Spearman correlations. The results were adjusted for age and body mass index. Statistical significance was considered for a bilateral value of p<0.05. Data are expressed by median (percentiles 25-75).

Results
• Mann-Whitney test: descriptive data

<table>
<thead>
<tr>
<th>Euthyroid group</th>
<th>SCH group</th>
<th>P</th>
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<tbody>
<tr>
<td>n=186</td>
<td>n=69</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>49 (36-60)</td>
<td>42 (30-58)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>26.56 (23.56-29.97)</td>
<td>25.51 (22.08-30.04)</td>
</tr>
<tr>
<td>TSH (μIU/ml)</td>
<td>1.45 (0.93-1.98)</td>
<td>3.60 (2.83-5.01)</td>
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<tr>
<td>FT4 (ng/dl)</td>
<td>1.02 (0.94-1.13)</td>
<td>1.00 (0.91-1.10)</td>
</tr>
<tr>
<td>FT3 (pg/ml)</td>
<td>2.73 (2.51-2.96)</td>
<td>2.85 (2.54-2.98)</td>
</tr>
<tr>
<td>Anti-TPO (UI/ml)</td>
<td>317.4 (62.0-1300.0)</td>
<td>317.6 (47.6-1300.0)</td>
</tr>
<tr>
<td>Anti-tg (UI/ml)</td>
<td>63.4 (28.6-147.5)</td>
<td>69.9 (26.7-175.4)</td>
</tr>
</tbody>
</table>

• Logistic regression: Risk factors to subclinical hypothyroidism, adjusted for age and BMI

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<thead>
<tr>
<th>OR (CI 95%)</th>
<th>p</th>
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<tbody>
<tr>
<td>Antithyroglobulin</td>
<td>1.002 (1.000-1.003)</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>1.008 (1.001-1.015)</td>
</tr>
<tr>
<td>CRP</td>
<td>1.684 (1.022-2.824)</td>
</tr>
</tbody>
</table>

• Spearman correlations: cardiovascular risk factors and thyroid function
• Total group:

  QUICKI  
  HOMA-IR  
  TSH  
  CRP
  WBISI  
  FT4  
  IGI  
  FT3  
  HDL

• Group with subclinical hypothyroidism:

Discussion
• We defined SCH from a TSH value of 2.5 μIU/ml because some studies have found that the mean population level of TSH is nearer the inferior limit considered nowadays normal.
• We found that patients with higher levels of total cholesterol have a statistically significant risk of having SCH.
• CRP is a marker of low grade inflammation and its increased values in patients with SCH may be related with the fact that atherosclerosis is considered an inflammatory process and its prevalence may be higher in SCH.
• We found that subjects with higher levels of anti-thyroglobulin antibodies have an increased risk of having SCH, and we found a positive correlation between FT4 levels and anti-TPO antibodies.
• Our findings suggest that SCH is a state of increased insulin resistance.

Conclusions
The interrelations between thyroid function, lipid profile, CRP and insulin-resistance demonstrate an increased cardiovascular risk in subclinical hypothyroidism due to autoimmune thyroiditis.