Ultrasonography of salivary glands in primary Sjögren’s syndrome. A comparison with magnetic resonance imaging and magnetic resonance sialography of parotid glands

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Objectives. To evaluate ultrasonography (US) of salivary glands in primary Sjögren’s syndrome (SS) and to compare US with parotid magnetic resonance (MR) imaging and MR sialography.

Methods. US examination of parotid, submandibular and sublingual glands was performed on 27 patients with primary SS, 27 healthy controls and 27 symptomatic controls without SS. The results were compared with parotid MR imaging and MR sialography and the clinical features of the patients.

Results. Salivary gland abnormalities, parenchymal inhomogeneity or adipose degeneration, were visualized in 21 (78%) SS patients, in one healthy control and in two symptomatic controls by US. Eighteen (67%) patients had changes in the parotid and submandibular glands and 8 (30%) changes in the sublingual glands. In the comparison, MR sialography was found to be the most sensitive method (96%), followed by MR imaging (81%) and US (78%), in detecting glandular changes. The specificity of US was 94%. The US and MR results were related to anti-Ro/SSA positivity but not to saliva secretion. The focus scores were related only to parotid MR imaging findings.

Conclusions. US, MR imaging and MR sialography with modern technology have reached such a good accuracy in visualizing glandular structural changes that they are promising alternatives to the conventional invasive examinations in the diagnostics of SS.

KEY WORDS: Diagnostics, Submandibular glands, Sublingual glands.

Subjects and methods

Subject characteristics

Twenty-seven consecutive outpatients with primary SS from the Division of Rheumatology at Oulu University Hospital constituted the patient group. The patients had to fulfil the American-European Consensus Group Classification Criteria for primary SS [30] to be eligible. Fifteen (55%) patients had a new and 12 a previous diagnosis of SS. The healthy control group consisted of 27 age- and sex-matched volunteers, mainly from among the medical staff of the hospital. The symptomatic control group consisted of 27 subjects with suspected SS. They had either sicca symptom (n = 25) and/or salivary gland swelling (n = 6), but they did not fulfil the international classification criteria for SS [30]. Subject characteristics are shown in Table 1. All patients and controls gave their informed consent. The study protocol was approved by the Ethical Committee of the University of Oulu.

Methods

Interviews and careful physical examinations, including Schirmer’s I test (mm/5 min) and unstimulated whole saliva sialometry...
patients had PIH or adipose degeneration of parotid glands (Table 2, Fig. 1), 18 (67%) PIH of the submandibular glands, and eight (30%) mild PIH (stage 1) of the sublingual glands. Two patients with PIH of the sublingual glands had normal parotid and submandibular findings. The findings were bilateral in all patients. One healthy control had adipose degeneration (stage 4) in her parotid glands and two symptomatic controls (one with sarcoidosis and one with Kartagener’s triad) had evident PIH (stage 2) in their parotid glands and mild PIH (stage 1) in their submandibular glands. Other controls had normal findings.

Comparison between glands. The parenchymal structural scores of parotid and submandibular glands were associated with each other ($r = 0.73$, $P < 0.0001$), while there was no relationship between the parenchymal stages of sublingual and parotid or sublingual and submandibular glands. There were three patients with normal parotids, but with stage 1 changes in either sublingual (two patients) or submandibular (one patient) glands.

The sensitivity of US was 78%, specificity 94%, accuracy 85%, positive predictive value 88% and negative predictive value 88%, if PIH and adipose degeneration (stages 1–4) were considered as a sign of primary SS. The kappa test for inter-observer variation was very good (0.83). The other salivary gland findings (hyperechoic bands, separate cysts or ducts, and the size of the gland) were not associated with the parenchymal classification and did not give any additional information for the diagnostics.

### Table 1. Characteristics of patients with primary Sjögren’s syndrome (SS), healthy controls and controls with sicca symptom or salivary gland swelling without SS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with SS (n=27)</th>
<th>Healthy controls (n=27)</th>
<th>Symptomatic controls without SS (n=27)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>n=27</td>
<td>n=27</td>
<td>n=27</td>
</tr>
<tr>
<td>Female/male</td>
<td>26/1</td>
<td>27/0</td>
<td>25/2</td>
</tr>
<tr>
<td>Schirmer’s I test ≤5 mm</td>
<td>21</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>UWSF ≤1.5 ml</td>
<td>25</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Focus score ≥1</td>
<td>14/14</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Anti-SSA/SSB</td>
<td>20</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Disease duration‡</td>
<td>28</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**Median.**

*In the symptomatic control group two patients had sarcoidosis, one had Kartagener’s triad, one had chronic idiopathic sialadenitis, eight had fibromyalgia, four had anxiety or depression, and six had medication prone to causing sicca symptoms ($\beta$-blocker, diuretic or antidepressant).

**Number of biopsies taken for this study. A biopsy was taken for diagnostic purposes only if it had not been taken earlier.

‡Years elapsed since the first symptom; sicca symptom or salivary gland swelling.

Hyper- and hypoechogenic areas of two–six mm; stage 1 = mild PIH (hypoechoic areas < 2 mm); stage 2 = evident PIH (hypoechoic areas of 2–6 mm); stage 3 = gross PIH (hypoechoic areas > 6 mm); and stage 4 = evident PIH (hypoechoic areas > 6 mm).

### Table 2. Structural classifications of parotid and submandibular glands by ultrasonography in patients with primary Sjögren’s syndrome

<table>
<thead>
<tr>
<th>Structure of parotid gland</th>
<th>Normal</th>
<th>Mild PIH</th>
<th>Evident PIH</th>
<th>Gross PIH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>8</td>
<td>1</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild PIH</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evident PIH</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross PIH</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adipose degeneration</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>7</td>
<td>10</td>
<td>1</td>
<td>27</td>
</tr>
</tbody>
</table>

* $r = 0.73$, $P < 0.0001$. 

**Statistical analysis**

SPSS 9.0 for Windows (SPSS, Chicago, IL, USA) was used for statistical analyses. The associations between continuous and ordinal variables were analysed by Spearman’s rank correlation.

**Comparison between glands.** The parenchymal structural scores of parotid and submandibular glands were associated with each other ($r = 0.73$, $P < 0.0001$), while there was no relationship between the parenchymal stages of sublingual and parotid or sublingual and submandibular glands. There were three patients with normal parotids, but with stage 1 changes in either sublingual (two patients) or submandibular (one patient) glands.

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### Results

**Ultrasonography**

**PIH and adipose degeneration.** Twenty-one (78%) patients had abnormal findings on US examination. Eighteen (67%) patients had abnormal findings on US examination. Eighteen (67%) patients had abnormal findings on US examination.
In a comparison of the US and MR methods, MR sialography seemed to be the most sensitive method (96%), followed by MR imaging (81%) and US [23].

The specificity of US was 94%. We could not assess the definitive specificity of MR methods reliably because they were only performed on seven healthy controls, although all controls had normal findings [23].

Heterogeneous, or nodular, parenchyma is considered the most accurate finding of SS patients’ salivary glands in both US and MR imaging. The finding of adipose degeneration differs significantly from the stages of PIH and cannot be graded by the same criteria. There are some previous data to show that this finding may be unspecific, as the amount of fat tissue increases in salivary glands with age [22, 32, 33] and in serum hyperlipidaemia [34, 35]. On the other hand, it has also been related to SS [21, 22], higher grades of X-ray sialography and focus score, and decreased saliva secretion [19, 21, 22]. Although we found one healthy control with adipose degeneration of parotid glands on US (MR imaging was not performed on her), the SS patients with such findings clearly showed features of advanced disease. They were all anti-Ro/SSA-positive and had manifestations of active systemic disease. Their focus score levels were higher (3.8 ± 1.7 vs 2 ± 1) and disease duration longer (8 ± 4.5 vs 3 ± 2.8), and they were younger (43 ± 10 vs 50 ± 14 yr) than the other patients. All these features together suggest that, although this finding is somewhat unspecific, it may also reveal the most advanced glandular disease stage in SS.

**US compared with MR**

Twenty-two (81%) patients with primary SS had abnormal parenchymal findings (nodular parenchyma or adipose degeneration) on MR images and 26 (96%) on MR sialography (ductal system changes or cavities) of parotid glands, while all the seven healthy controls had normal findings. These results have been described in more detail earlier [23]. The parenchymal scores of parotid glands on US and MR images were closely related to each other ($r = 0.76$, $P < 0.0001$).

**Clinical associations**

The presence of anti-Ro/SSA and/or anti-La/SSB antibodies was associated with the parenchymal findings on parotid MR imaging ($P < 0.01$) and US ($P < 0.05$), but not with submandibular or sublingual US. The focus scores of the 15 SS patients with a recent duration, the presence or number of systemic disease complications was not significant. The results of neither US nor MR methods, MR sialography seemed to be the most sensitive method (96%), followed by MR imaging (81%) and US [23].

The specificity of US was only seen in parotid glands. The sublingual glands seemed to be less severely affected, although two patients with mild PIH of the sublingual glands had normal parotid and submandibular findings. Thus, to achieve the best sensitivity of US, all salivary glands should be examined. In a comparison of the US and MR methods, MR sialography seemed to be the most sensitive method (96%), followed by MR imaging (81%) and US [23].

**Discussion**

Abnormal findings (either PIH or adipose degeneration) were found in 21/27 (78%) patients, and in 1/27 (4%) healthy and 2/27 (7%) symptomatic controls in US of salivary glands. The findings of parotid and submandibular glands were in concordance with each other and were equally frequent, although adipose degeneration was only seen in parotid glands. The sublingual glands seemed to be less severely affected, although two patients with mild PIH of the sublingual glands had normal parotid and submandibular findings. Thus, to achieve the best sensitivity of US, all salivary glands should be examined. In a comparison of the US and MR methods, MR sialography seemed to be the most sensitive method (96%), followed by MR imaging (81%) and US [23].
Roles of US, MR imaging and MR sialography in the diagnosis of SS

US, MR imaging and MR sialography visualize the salivary gland in its physiological state without artefacts caused by intraductal contrast media or biopsy procedures, not to mention the lack of inconvenience and risk of complications to the patient. With modern equipment, they can yield such a definitive picture of the glandular structural changes that they are promising alternatives to conventional examinations, and their use is likely to increase both in clinical practice and in scientific research in the near future. However, comparative multicentre studies should be conducted to confirm their diagnostic value and cost-effectiveness in SS before they can be widely accepted and included in the classification criteria of SS.

According to the available data, US is a good candidate for a first-line radiological examination in the diagnosis of SS, because it is much cheaper and more widely available than MR and gives an opportunity to evaluate all salivary glands easily at the same time. However, it should be kept in mind that US is operator-dependent, and the examinations should be centralized to radiologists who are experienced in soft tissue US. MR sialography and MR imaging, combined with MR sialography and computed tomography of the salivary glands in the evaluation of Sjögren’s syndrome. Comparison with parotid sialography. J Rheumatol 1988;15:1777–81.


