CHAPTER 5

Salivary imaging
SUMMARY

Aim - Sialography is commonly used for the purpose of diagnosing Sjögren's syndrome, though its invasive nature is often regarded as a serious drawback for routine usage. The aim of this study was to evaluate the morbidity and acceptability of parotid sialography using oil-based contrast fluid.

Methods - Twenty-four consecutive sialographic procedures were evaluated by assessing the morbidity and patient's acceptance of the procedure with a standardised questionnaire, and by recording relevant physical parameters during the procedure.

Results - There was good acceptance of the sialographical procedure, and the morbidity was low. No signs of overfilling or fausse route were observed in any of the sialograms. On average, 0.74 ml contrast fluid was infused at a velocity of 0.01 ml/s. The whole procedure was completed within 12 minutes.

Conclusions - Parotid sialography appears less invasive than is often thought. It has a low morbidity and is well accepted by the patients.
MORBIDITY FROM PAROTID SIALOGRAPHY


Department of Oral and Maxillofacial Surgery, University Hospital Groningen


INTRODUCTION

Introduced early in the previous century, sialography has proven a useful technique throughout the years. Through retrograde infusion of oil- or water-based iodine contrast, the architecture of the salivary duct system is visualised radiographically. There is debate ongoing in the literature regarding the current value of contrast sialography for the clinical differentiation of salivary gland disorders. Due to the availability of new imaging procedures, such as MRI, CT scanning, scintigraphy and ultrasonography, its diagnostic indication has significantly been narrowed and limited to imaging of the ductal system. For the purpose of diagnosing Sjögren's syndrome, sialography is still commonly used, as it has been proven to reveal characteristic changes of the salivary gland ductal system with rather high sensitivity and specificity.

Following the introduction of water-based contrast fluids in the 1950's, these fluids have been advocated in sialography for their better tolerance in the human body having a physicochemical composition closer to body fluids. A comparative study between oil-based and water-based contrast revealed no adverse reactions with both contrast media. Nevertheless, invasiveness and poor tolerance is by some clinicians considered a drawback for routine usage of oil-based sialography, especially in SS patients. To date, however, the subjective experiences of the patients have not been described. The aim of this study was to evaluate the morbidity and acceptability of oil-based contrast sialography.

PATIENTS AND METHODS

Patients
Twenty-four consecutive patients who had undergone parotid contrast sialography for the diagnosing of Sjögren's syndrome in the period from October 1999 until April 2000 at the Department of Oral and Maxillofacial Surgery of the University
Hospital Groningen participated in this study. The studied group comprised 22 women and 2 men (mean age of 57 years; SD 9; range 41 to 75). The right parotid gland was used 21 times and the left parotid gland three times. Iodine allergy was applied as an exclusion criterion for the study, since iodine is present in the contrast fluid used. No patients had to be excluded from the study.

Technical procedure for sialography
All sialograms were obtained in absence of acute sialadenitis. If clinical signs of acute inflammation were present, sialography was postponed until clinical signs had subsided for at least six weeks. Parotid sialograms were made unilaterally (preferably of the right gland) in a standardised manner. Reasons for using the left parotid gland included probing difficulties and asymmetrical parotid gland swelling. All sialograms were made by the same clinician. After cannulation of the parotid main duct, the gland was filled through retrograde infusion of an oil-based contrast fluid (Lipiodol U.F.®), under low pressure¹⁵ using a 2-ml Cornwall® syringe (Becton Dickinson). The patient’s sensation of a sudden increase of pre-auricular pressure was used to estimate the proper filling level of the gland, after which two pictures (posteroanterior and lateral) were made. Premature leakage of contrast fluid was prevented through main duct ligation under local anaesthesia. A General Electric G1000 was used as X-ray apparatus; pictures were made with an additional filter with 58 kV during 0.18 s. After removal of the ligature and massaging the parotid gland patients were advised to stimulate salivary gland secretion with citric flavoured gum or candy during the first hours, in order to enhance wash out of remaining contrast fluid.

Evaluation of the procedure
The sialographical procedure was evaluated by an independent investigator using the following two methods: assessment of relevant physical parameters during the procedure and a standardised patient questionnaire. There was no time interval between the making of the sialogram and the subsequent evaluation, with the exception of the duration of pain sensation after the procedure and the overall judgement, which were recorded at a recall visit after three weeks. As physical parameters, the duration of the whole procedure, the duration of contrast infusion and the total amount of infused contrast fluid were recorded. The velocity of contrast infusion was in addition calculated. The questionnaire contained multiple choice questions about presence and severity of pain during the sialographical procedure, duration of pain following sialography, and the patients’ acceptance of
the procedure. Pain severity was graded on a visual analogue scale (0 representing no pain, 10 representing severe pain).

**RESULTS**

Physical parameters of sialography
The duration of the whole procedure averaged 12 minutes (mean 716 s, SD 186 s, range 552 - 955 s). The volume of infused contrast fluid averaged 0.74 ml (SD 0.08 ml, range 0.50 - 0.90 ml), whereas the mean velocity of infusion was calculated at 0.01 ml/s (SD 0.001ml/s, range 0.008 - 0.013 ml/s). There was no evidence of leakage of contrast medium into the oral cavity until the ligature was removed. Radiographically, all sialograms showed good filling of the gland; no fausse route was observed.

Morbidity and acceptability
Twenty-four sialographical procedures were evaluated in twenty-four patients. Nineteen of 24 patients experienced no pain during infusion of the contrast fluid, whereas 5 patients experienced little pain. The pain severity during the procedure averaged 4.0 in latter patients.
Sixteen of 24 patients experienced 'no discomfort' during the sialographical procedure, 7 patients found it 'a little unpleasant' and one patient found it 'very unpleasant'. To the question, which part of the procedure was experienced as the most unpleasant sensation, surprisingly, patients stated most often it was the opening of the mouth (n=7), instead of the placement of the ligature (n=2) or the infusion of contrast fluid (n=2).
Fifteen patients had no pain at all after the procedure and 5 felt soreness for one day. Two patients stated that a sore feeling had lasted about a week whereas two had a sore feeling nearby the parotid region lasting about two weeks.
To estimate the subjective acceptability of the sialographical procedure, the patients were requested to judge the procedure using a number between 0 and 10, with 0 indication 'very bad experience' and 10 'no problems at all'. The judgement averaged 8.7.
DISCUSSION

Most of the patients experienced no pain or discomfort during sialography (79% and 67%, respectively). The average patient judgement of the procedure was very high.

The mild pain that was felt by 5 of the patients during the contrast infusion was most likely related to the perception of raised intraluminal pressure or distension of the parotid capsule from minor glandular enlargement.

Soreness in the parotid region for a short period after parotid sialography, as occurred in a few patients, may relate to presence of some residual contrast fluid in the gland, especially in cases of sialectasia. Another explanation for the temporary soreness might be the presence of a subclinical sialadenitis prior to sialography, rendering the gland more sensitive to contrast fluid. The two patients who felt pain for longer than a week both have been examined by their general practitioner, who concluded that other reasons than sialography had been responsible for their complaints (sinusitis and headache, respectively).

Though sialography is considered the imaging procedure of choice for diagnosing Sjögren’s syndrome, it should not be performed in case of iodine allergy to prevent local and systemic allergic reactions. Alternative positive contrast materials for iodine, such as barium-sulphate suspensions, are not suitable for sialography due to a large particle size. Therefore, if confronted with patients with a history of iodine allergy, other imaging techniques such as scintigraphy or ultrasonography should be used instead to visualise salivary gland pathosis. Regarding the use of CT and MRI techniques in diagnosing SS, conflicting results have been reported in literature.

Though the use of oil-based contrast fluid has often been associated in literature with non-allergic adverse tissue responses or even with damage to the gland, we have experienced no complications whatsoever during or after sialography. We feel that, if lipiodol is restrained to the ductal lumen during the procedure, no adverse tissue effects can be expected. Lipiodol remains, due to its hydrophobic nature, much better within the salivary ducts, than water-based contrast fluids that pass more easily through the ductal epithelium. As a result, the clearance of contrast fluid differs substantially between oil- and water based contrast. Oil-based fluid leaves the gland with saliva secretion via the main salivary duct, whereas water-based fluid diffuses across the ductal epithelium and is cleared subsequently from the circulation by kidneys and liver. Therefore, one might actually expect less adverse reactions from oil-based contrast than from water-based contrast in the normal situation. Only if a iatrogenic fausse route is induced during contrast infusion, is a less favourable tissue response to be expected from oil-based contrast,
since in such situation it remains in the gland parenchyma for a long time inducing a chronic granulomatous inflammation, as opposed to quick clearance of water-based contrast in the same situation. If uncertain about the ductal probing or if inexperienced with contrast sialography, it seems wise therefore to use water-based contrast fluids. This way, adverse tissue reaction from a possible fausse route or overfilling is minimised.

The use of oil-based contrast, whose hydrophobic nature impairs the fluid’s ability to mix with saliva or to pass through epithelial membranes of the salivary ducts, renders much sharper X-ray images than water-based alternatives. Therefore, we prefer the use of lipiodol or other oil-based contrast fluids, yielding optimum quality of sialographical images with, in our hands, no adverse side effects on the salivary glands of any kind.

Given its low morbidity and its subjective acceptability, sialography of the parotid gland appears, if performed properly, to be less invasive than is often thought. With some practice, this diagnostic imaging technique can be applied in ten to fifteen minutes, differentiating between a variety of salivary gland disorders including Sjögren’s syndrome.

REFERENCES

Chapter 5.2

SUMMARY

Aim - Despite the availability of many new imaging procedures, sialography has, after decades of use, maintained its status as the imaging procedure of choice for evaluating the oral component of Sjögren's syndrome (SS). In this study, the clinical value of sialography as a diagnostic tool in SS was explored by assessing its diagnostic accuracy, observer bias and staging potential.

Methods - One hundred parotid sialograms were interpreted independently in a blind fashion by two trained- and two expert-observers. Sialograms were derived from a group of consecutive patients, referred for diagnostics of SS. Patients were categorised as SS and non-SS by the revised European classification criteria.

Results - Trained observers reached a sensitivity of 95 and a specificity of 33 percent for SS by sialogram, whereas expert-observers reached a sensitivity of 87 and a specificity of 84 percent. There was only 'fair' inter-observer agreement between trained- and expert-observers, whereas both expert-observers showed 'good' agreement with one another, according to Cohen's kappa. Intra-observer agreement was 'good' to 'very good' for all observers. The four different gradations of sialectasia, i.e. punctate, globular, cavitary and destructive, showed a weak but significant correlation with the duration of oral symptoms.

Conclusions - This study markedly shows that the diagnostic value of parotid sialography for diagnosing SS greatly depends upon the skills of the observer, implying that sialography lacks general applicability as a diagnostic tool in SS and requires specific expertise. Nevertheless, given its potentially high sensitivity and specificity in diagnosing SS as well as its useful staging potential, sialography still has its use in the evaluation of the oral component of SS.
Parotid sialography for diagnosing Sjögren’s Syndrome

W.W.I. Kalk¹, A. Vissink¹, F.K.L. Spijkervet¹, H. Bootsma², C.G.M. Kallenberg³, J.L.N. Roodenburg¹

Departments of ¹Oral and Maxillofacial Surgery, and Internal Medicine, divisions of ²Rheumatology, and ³Clinical Immunology, University Hospital Groningen

Submitted for publication

Introduction

Sjögren’s syndrome (SS) is considered a systemic autoimmune disease with the exocrine glands as main target-organs. As a result, the presence of this disease may cause structural damage and secretory dysfunction of the tear- and salivary glands. The tear- and salivary gland involvement with its inherent morbidity is often addressed as the ocular- and the oral component of SS, respectively.

The oral component of SS can be evaluated in many ways. Generally, two different procedures are practised, i.e. assessment of salivary gland function and salivary gland imaging. Salivary gland function is assessed through measurement of salivary secretion rate (sialometry) and analysis of salivary composition (sialochemistry).¹⁻³

Salivary gland imaging is currently performed by several procedures including magnetic resonance imaging (MRI), computer tomography (CT) scanning, ultrasonography, scintigraphy and sialography.⁴⁻⁹ Despite the availability of new imaging procedures, the oldest procedure of all, sialography has maintained its status as the method of choice for exploring the ductal system of the salivary gland to diagnose SS.¹⁰

Sialography reveals the architecture of the salivary duct system radiographically by insertion of a contrast fluid. This radiographic demonstration of salivary glands in vivo was first performed in 1913.¹¹ Four decades ago the sialographic changes seen on sialograms were accurately described and, with regard to chronic sialadenitis, classified into punctate, globular, cavitory and destructive sialectasia (dilatation) of the acinar and ductal system.¹²⁻¹⁴ These four sialectatic changes are thought to represent increasing glandular damage, respectively, caused by chronic salivary gland inflammation.¹⁴ SS is by far the most frequent cause of such chronic salivary gland inflammation. Therefore, by observing sialectasia on a sialogram, the presence (and progression) of SS with regard to its oral component can be determined.
It has been demonstrated that SS-related sialographic findings such as sialectasia are more closely related to SS-related clinical symptoms (stimulated parotid salivary flow, incidence of keratoconjunctivitis sicca) than is the periductal lymphocytic infiltration of the labial glands. In addition, superior sensitivity and/or specificity for SS have been frequently ascribed to sialography as compared to labial gland biopsy. However, the subjective nature of reading and interpreting a sialogram causes a certain observer bias, as is the case with diagnostic-imaging tests in general. The amount of observer bias may have a substantial impact on the clinical value of a particular diagnostic test.

In this study the clinical value of sialography as a diagnostic tool in SS was explored by assessing its diagnostic accuracy, observer bias and staging potential in 100 sialograms.

PATIENTS AND METHODS

Patients

In order to study the clinical value of sialography for diagnosing Sjögren’s syndrome (SS) 100 parotid sialograms were interpreted independently by four observers. Two observers had large general experience in judging sialograms, whereas two observers were in addition especially experienced in the judging of sialograms with respect to the diagnosis SS. The observers with general experience are termed ‘trained observers’ and the observers with specific SS expertise are termed ‘expert-observers’. Sialograms were derived from a non-selected group of 100 consecutive patients referred to the outpatient clinic of the Department of Oral and Maxillofacial Surgery of the University Hospital Groningen in the period from December 1997 until August 1999.

Patients suspected of SS were referred by rheumatologists, internists, neurologists, ophthalmologists, ENT-specialists, general practitioners and dentists. Reasons for referral included mouth-dryness, eye-dryness, swelling of the salivary glands, arthralgia and fatigue. The diagnostic work-up for SS, carried out in all patients, included the following aspects: subjective complaints of oral and ocular dryness (table 3.1.1), sialometry and sialochemistry, histopathology of salivary gland tissue, serology (SS-A- and SS-B antibodies) and eye tests (Rose Bengal staining and Schirmer tear test). Sialography was excluded for diagnostic use in this study, in order to avoid an incorporation bias. In addition to the diagnostic tests, the duration of oral symptoms and the serum level of immunoglobulin class G (IgG) were assessed in order to be studied in relation to the sialographical stage. Duration of
oral symptoms was defined as the time from first complaints induced by or related to oral dryness until referral. In this study, the revised European classification criteria for SS\(^{24,25}\) were used as reference standard for the diagnosis of SS, categorising patients as primary SS, secondary SS, or non-SS patients.

Exclusion criteria
Iodine allergy was applied as an exclusion criterion for the study, since iodine is present in the contrast fluid used. Furthermore, the exclusion criteria of the European classification criteria for SS were applied. Psoriatic arthritis and HIV-infection were excluded as both diseases may cause sialographical pictures resembling SS.\(^{26-33}\) No patients had to be excluded from the study.

Technical procedure for sialography
All sialograms were obtained in absence of acute sialadenitis. If clinical signs of acute inflammation were present, sialography was postponed until clinical signs had subsided for at least six weeks. Parotid sialograms were made unilaterally (preferably of the right gland) in a standardised manner. All sialograms were made by the same clinician. After cannulation of the parotid main duct the gland was filled through retrograde infusion of an oil-based contrast fluid (lipiodol U.F.) using a 2-ml Cornwall syringe\(^\circledR\) (Becton and Dickinson). The patient's sensation of a sudden increase of pre-auricular pressure was used to estimate the proper filling level of the gland. Premature leakage of contrast fluid into the mouth was prevented through main duct ligation under local anaesthesia. A General Electric G1000 was used as X-ray apparatus; posteroanterior (6° mediolateral) and lateral pictures were made with an additional filter with 58 kV during 0.18 s. After removal of the ligature and massaging the parotid gland patients were advised to stimulate salivary gland secretion with citric flavoured gum or candy during the first hours in order to enhance wash out of the remaining contrast fluid. The whole procedure was completed within 15 minutes.

Evaluation of the sialograms
Four observers each examined independently 100 sialograms in a random order with no information from the patients other than the reason for referral (clinical suspicion of SS) and the amount of inserted contrast fluid. Of the 100 sialograms, 25 were judged a second time by all observers without being aware of it, in order to determine intra-observer variability. All sialograms were examined in the presence of
an independent investigator who made sure that each set of sialograms was examined within 2 minutes without being revised afterwards.

Before the observers examined the sialograms, a calibration session took place in which all observers agreed upon the criteria to be applied when describing the sialograms. Four different pathological descriptions were agreed upon. The observers had to determine whether or not these patterns were present in each sialogram. These patterns were sialectasia (subdivided into punctate, globular, cavitary and destructive), thin appearance of the ducts with or without gland enlargement, irregular and widened main ducts, and presence of a space-occupying lesion, respectively.

Figure 5.2.1 Stages of sialectasia in SS, as present on lateral parotid sialograms:
- punctate sialectasia (A): less than 1 mm in size;
- globular sialectasia (B): uniform of shape and 1-2 mm in size;
- cavitary sialectasia (C): irregular of shape and more than 2 mm in size;
- destructive sialectasia (not shown): complete loss of gland architecture.
If present, sialectasia (dilatations) were graded according to the description by Blatt: punctate if less than 1 mm in size; globular if uniform and 1-2 mm in size; and cavitary if irregular and more than 2 mm in size (figure 5.2.1). A destructive pattern was defined as complete destruction of the gland architecture, simulating an invasive neoplastic process. Sialectasia were considered the only descriptions suggestive for a diagnosis of SS. Presence of thin ducts was regarded as possibly consistent with sodium retention dysfunction syndrome or with sialoadenosis. Irregular and widened main ducts consistent with sialodochitis (salivary duct inflammation) were considered the prevalent feature in chronic-recurrent sialadenitis. A space-occupying lesion on a sialogram was considered suggestive for a tumour compressing the gland. A consensus judgement whether or not a sialogram is in accordance with the diagnosis SS was based upon the majority of the individual descriptions of the observers.

Statistical analysis
Data were submitted for statistical analysis using the Statistical Package for the Social Sciences (SPSS), version 9.0. The following statistical procedures were applied: Cohen’s kappa as measure of inter- and intra-observer agreement (observer bias), and Pearson’s and Spearman’s coefficients as correlation tests. In the results section it is stated which statistical test was applied in a specific situation. A significance level of 0.05 was pre-defined in all cases.

RESULTS

Study group
By applying the revised European classification criteria for Sjögren’s syndrome (SS) on the studied cohort, 39 patients were categorised as SS (20 primary- and 19 secondary SS; male/female ratio: 1/7; mean age of 54 years; SD 15; range 21 to 84) and 61 patients as non-SS (negative for SS) (male/female ratio: 1/14; mean age of 54 years; SD 15; range 20 to 81). The latter were, based upon additional clinical and laboratory tests, diagnosed as having sialoadenosis (n=18), sodium retention dysfunction syndrome (n=18), medication induced xerostomia (n=11), or as having no alternative disease directly related to salivary gland pathology (n=14). Mean duration of oral symptoms before referral was 35 months for SS- and 30 months for non-SS patients (range: SS 0-180 months, non-SS 0-240 months).
Test accuracy for SS

By determining the presence of sialectasia as diagnostic indicator for SS, the sensitivity and specificity differed greatly between the trained- and expert-observers. Trained observers reached a sensitivity of 95 and a specificity of 33 percent, whereas expert-observers reached a sensitivity of 87 and a specificity of 84 percent (table 5.2.1). The large difference in specificity between trained- and expert-observers was mainly due to their decision when doubting between ‘no abnormality’ and ‘punctate sialectasia’. Examples of sialograms that gave rise for doubt are illustrated in figures 5.2.2 and 5.2.3.

Figure 5.2.2
Example of a parotid sialogram of a SS-patient, which could give rise for doubt. Note the presence of initial sialectasia on both projections. All observers judged this sialogram as positive for SS (sialectasia present).

Figure 5.2.3
Parotid sialogram of a non-SS patient. Note the small radiodensities that could be easily misinterpreted. Experienced observers judged this sialogram as positive, whereas expert observers as negative for SS (no sialectasia present).
Expert-observers, reached a high specificity by choosing ‘no abnormality’ in case of doubt (observers A and B), whereas trained observers, who chose for ‘punctate sialectasia’ in the same situations, suffered from a major drop in specificity and gained only slight improvement of sensitivity (observers C and D). Consequently, the likelihood ratios also greatly differed between trained- and expert-observers, varying from 1.2 (not very useful as a test) to 5.0 (very useful as a test). Consensus judgement based upon the majority of individual judgements reached an intermediate sensitivity and specificity for SS of 92 and 71 percent, respectively, and a likelihood ratio of 3.1. In 18 of the 61 non-SS patients, sialectasia was present on the sialogram, according to consensus judgement (table 5.2.2).

Expert-observers, reached a high specificity by choosing ‘no abnormality’ in case of doubt (observers A and B), whereas trained observers, who chose for ‘punctate sialectasia’ in the same situations, suffered from a major drop in specificity and gained only slight improvement of sensitivity (observers C and D). Consequently, the likelihood ratios also greatly differed between trained- and expert-observers, varying from 1.2 (not very useful as a test) to 5.0 (very useful as a test). Consensus judgement based upon the majority of individual judgements reached an intermediate sensitivity and specificity for SS of 92 and 71 percent, respectively, and a likelihood ratio of 3.1. In 18 of the 61 non-SS patients, sialectasia was present on the sialogram, according to consensus judgement (table 5.2.2).

Observer agreement
Inter- and intra-observer agreement was calculated for the four pathological conditions that were determined on the sialograms by each observer. With regard to the presence of SS (sialectasia as indicator), there was only ‘fair’ inter-observer agreement between trained- and expert-observers, whereas both expert-observers showed ‘good’ agreement with one another, according to Cohen’s kappa. The intra-observer agreement was ‘good’ to ‘very good’ (table 5.2.3). The determination of other sialographical alterations that occur in sialoadenosis, sialodochitis and salivary

**Table 5.2.1. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratio (LR) of the four observers (expert: A, B; trained: C, D) for the diagnosis of SS on a group of 100 patients by presence of sialectasia on the sialogram. Consensus judgement was based upon the majority of individual judgements for each sialogram. Note the large differences between expert- and trained observers regarding specificity and likelihood ratio.**

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th></th>
<th>B</th>
<th></th>
<th>C</th>
<th></th>
<th>D</th>
<th></th>
<th>consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>87%</td>
<td></td>
<td>82%</td>
<td></td>
<td>95%</td>
<td></td>
<td>92%</td>
<td></td>
<td>92%</td>
</tr>
<tr>
<td>Specificity</td>
<td>71%</td>
<td></td>
<td>84%</td>
<td></td>
<td>33%</td>
<td></td>
<td>23%</td>
<td></td>
<td>71%</td>
</tr>
<tr>
<td>PPV</td>
<td>65%</td>
<td></td>
<td>76%</td>
<td></td>
<td>47%</td>
<td></td>
<td>43%</td>
<td></td>
<td>67%</td>
</tr>
<tr>
<td>NPV</td>
<td>90%</td>
<td></td>
<td>88%</td>
<td></td>
<td>91%</td>
<td></td>
<td>82%</td>
<td></td>
<td>94%</td>
</tr>
<tr>
<td>LR</td>
<td>3.0</td>
<td></td>
<td>5.0</td>
<td></td>
<td>1.4</td>
<td></td>
<td>1.2</td>
<td></td>
<td>3.1</td>
</tr>
</tbody>
</table>

**Table 5.2.2. Judgements of 100 sialograms regarding the presence and grade of sialectasia by four individual observers (expert: A, B; trained: C, D) and by consensus. For each descriptive category the number of cases accordingly judged is given. Consensus judgement is based upon the majority of individual judgements for each sialogram. Note the large variability between expert- and trained observers regarding false positivity: the trained observers judged many sialograms from non-SS patients as punctate.**

<table>
<thead>
<tr>
<th>Sialectasia</th>
<th>SS</th>
<th>non-SS</th>
<th>SS</th>
<th>non-SS</th>
<th>SS</th>
<th>non-SS</th>
<th>SS</th>
<th>non-SS</th>
<th>SS</th>
<th>non-SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>5</td>
<td>43</td>
<td>7</td>
<td>51</td>
<td>2</td>
<td>20</td>
<td>3</td>
<td>14</td>
<td>3</td>
<td>43</td>
</tr>
<tr>
<td>punctate</td>
<td>13</td>
<td>5</td>
<td>15</td>
<td>1</td>
<td>11</td>
<td>24</td>
<td>12</td>
<td>36</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>globular</td>
<td>11</td>
<td>6</td>
<td>10</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>15</td>
<td>5</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>cavitory</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>15</td>
<td>8</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>destructive</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Observer agreement
Inter- and intra-observer agreement was calculated for the four pathological conditions that were determined on the sialograms by each observer. With regard to the presence of SS (sialectasia as indicator), there was only ‘fair’ inter-observer agreement between trained- and expert-observers, whereas both expert-observers showed ‘good’ agreement with one another, according to Cohen’s kappa. The intra-observer agreement was ‘good’ to ‘very good’ (table 5.2.3). The determination of other sialographical alterations that occur in sialoadenosis, sialodochitis and salivary
gland tumour all suffered from rather low inter-observer agreement, varying from ‘poor’ to ‘moderate’ (data not shown).

<table>
<thead>
<tr>
<th>Inter-observer agreement</th>
<th>N=100</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>-</td>
<td>0.762</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B</td>
<td>0.386</td>
<td>0.339</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C</td>
<td>0.322</td>
<td>0.258</td>
<td>0.588</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intra-observer agreement</th>
<th>N=25</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.824</td>
<td>0.874</td>
<td>0.839</td>
<td>0.762</td>
<td></td>
</tr>
</tbody>
</table>

Staging potential
The different gradations of sialectasia (figure 5.2.1) showed a weak but significant correlation with the duration of oral symptoms in SS patients ($r_{\text{pearson}}$ 0.29, $p<0.05$). According to consensus judgement of the sialograms, the observation of punctate sialectasia corresponded with an average duration of oral symptoms of 15 months, whereas globular-, cavitary- and destructive sialectasia corresponded with increasing duration of 39, 44 and 59 months, respectively. No relation was observed between the serum level of immunoglobulin class G (IgG) and the presence or gradation of sialectasia in SS patients.

Volume lipiodol
The gradation of sialectasia related significantly to the amount of lipiodol that was infused into the parotid gland with sialography ($r_{\text{pearson}}$ 0.26, $p<0.01$). On average, 10% more lipiodol fluid had been infused in the parotid gland of SS patients compared to non-SS patients ($0.81\pm0.20$ ml versus $0.73\pm0.10$ ml lipiodol, T-test: $p<0.05$). In agreement with this, on average 20% less lipiodol had been infused if thin ducts were observed ($0.66\pm0.08$ ml versus $0.79\pm0.15$ ml lipiodol, T-test: $p<0.01$).

Ductal changes
The presence of widened or irregular main ducts, consistent with sialodochitis, was not diagnostic for SS (sensitivity 28%, specificity 62%, likelihood ratio 0.7), and was neither related to salivary flow rates nor to duration of oral complaints. The observation of thin ducts with or without salivary gland enlargement, regarded as possibly consistent with sialoadenosis or sodium retention dysfunction syndrome,
did not relate significantly to any changes of salivary composition (e.g. sodium, potassium, amylase, total protein), nor to salivary flow rate.

**DISCUSSION**

It has become clear from this study that it is possible to achieve both a sensitive and specific test result with parotid contrast sialography for diagnosing SS (likelihood ratio up to 5.0). This diagnostic accuracy, however, is very much dependant on the observer involved, which implies that the technique lacks general applicability and requires specific expertise.

The four different gradations of sialectasia showed a weak but significant relation to the duration of oral symptoms in SS patients, suggesting that sialectasia slowly worsens (increases in number and size) during the disease course of SS. Previous studies have already shown that, in SS patients, increasing gradations of sialectasia correspond with lower salivary flow rates\(^3,15,42\), as well as that salivary flow rates deteriorate with increasing duration of oral symptoms (§3.1).\(^43\) We therefore suggest that SS can be subdivided into different sequential stages according to the type of sialectasia on the sialogram, with a corresponding degree of hyposalivation.

Though the use of oil-based contrast fluid has often been associated in literature with high rates of complications, we have experienced none of the complications associated with oil-based contrast fluids during or after the one hundred sialograms performed. Since the use of oil-based contrast fluid does result in superior image quality, we prefer oil-based contrast fluid above water-based alternatives for use in sialography, in case of well-trained clinicians. Otherwise, a water-based contrast fluid is advisable. In case of iodine allergy, sialography should not be performed to prevent local and systemic allergic reactions. Alternative positive contrast materials other than iodine that are currently in use are not suitable for sialography. Therefore, in cases of iodine allergy other imaging techniques such as scintigraphy or ultrasonography should be used instead to visualise salivary gland involvement in SS. Conflicting results have been reported in literature regarding the use of CT and MRI techniques in diagnosing SS.\(^4,5,8\)

Though some studies have reported abnormal parotid sialographic findings as a fairly common finding in control subjects (up to 40%)\(^8,44,45\), sialography is generally considered a very specific diagnostic test for SS.\(^20-23\) However, sialectasia, may also occur singly as result of chronic-recurrent parotitis, a condition unrelated to SS.\(^38,39\) The latter may perhaps account for at least some of the sialectasia we observed in 30% of the non-SS patients. Furthermore, some of the observed sialectasia in non-SS
patients probably has to be attributed to observer error, since the number of false positive cases varied markedly between trained- and expert-observers. The observer’s decision, especially when in doubt about recognising initial sialectasia at the beginning of SS, reflects crucially upon the test specificity, i.e. the number of false positive cases (tables 5.2.1 and 5.2.2, figures 5.2.2 and 5.2.3). Other imaging procedures, however, may well suffer from the same human factor, i.e. subjectivity and varying expertise with interpreting the image.
Since diagnostic testing for SS is performed in the second echelon, there is an increased prior chance for SS compared to the general population. Furthermore, the diagnosis SS is based upon several diagnostic tests. Both the raised prior chance for SS and the combined-test approach require diagnostic tests with emphasis on specificity. For this reason, it is recommended that one chooses negatively when in doubt about the presence of sialectasia on a sialogram (as illustrated in figures 5.2.2 and 5.2.3), thereby increasing the specificity of the test result. The diagnostic accuracy of sialography might be further improved with a digital subtraction technique that eliminates osseous background structures, and thus offers interference-free visualisation of glandular structures. Such enhancement of image quality might not only reduce the number of false positive test-results, but also significantly improve the inter-observer agreement. Negative aspects of this procedure are its sensitivity to patient movement (swallowing, tongue movement) during contrast injection and the need for advanced X-ray equipment.

In conclusion, reading and interpreting a sialogram requires certain expertise with regard to the recognition and correct interpretation of first stage sialectasia, restricting its use as a diagnostic tool for incipient SS to expert-observers. In cases of doubt, one should therefore consider sending the (digitised) sialogram to an expert centre. Despite limited general applicability, sialography still has its unique value in the evaluation of SS. Its costs are low and, if interpreted properly, it is highly diagnostic. Furthermore, it has a relatively low degree of invasiveness and it is a relatively simple and quick procedure (§5.1). The time-relation of the progression of sialectasia renders sialography an especially valuable tool in SS with regard to the assessment of disease progression.

**Acknowledgements**

The advice and support of Dr. B. Stegenga (Oral and Maxillofacial Surgeon, Epidemiologist, University Hospital Groningen) and Dr. J. Schortinghuis (Research
Associate dept. of Oral and Maxillofacial Surgery, University Hospital Groningen) are gratefully acknowledged.

REFERENCES
