Ultrasound Supplemented by Sialendoscopy: Diagnostic Value in Sialolithiasis

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Abstract

Objective. To assess the value of ultrasound, if indicated, supplemented by sialendoscopy, in the diagnosis of sialolithiasis.

Study Design. Retrospective study.

Setting. Referring center for salivary gland diseases.

Subjects and Methods. All patients who presented with a suspected diagnosis of obstructive sialopathy between January 2011 and April 2017 and had not undergone any treatment were retrospectively evaluated. A total of 2052 patients and 2277 glands were included in the study. Ultrasound examinations were carried out initially and followed by sialendoscopy in all cases. Direct demonstration of sialolithiasis by sialendoscopy, transoral ductal surgery, and discharge of concrements/observation of fragments during sialendoscopy after extracorporeal shock-wave lithotripsy were regarded as definitive evidence of sialolithiasis.

Results. Ultrasound had an accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of 94.77%, 94.91%, 94.57%, 96.14%, and 92.89%, respectively, for the diagnosis of sialolithiasis. All false-positive findings were correctly diagnosed, and in all false-negative findings, stones/fragments were visualized by sialendoscopy. Over 95% of the false-negative findings in major salivary glands (64/67) had visible ductal dilation in sonography, and in 73.1%, the stones not detected on ultrasound were located in the distal part of the duct, which is easily accessible with the sialendoscope.

Conclusion. This study shows that sialolithiasis can be diagnosed using ultrasonography with a high degree of certainty. If supplemented by sialendoscopy, the correct diagnosis could be established in virtually all cases of sialolithiasis. Ultrasound supplemented by sialendoscopy has the potential to serve as an alternative diagnostic standard in the future.

Keywords
salivary, stones, glands, submandibular, parotid, ultrasound, sialolithiasis, sialendoscopy

Sialolithiasis is the most frequent cause of obstructive sialadenopathy.1-4 Over 50% of salivary stones cannot clinically be reliably assessed by palpation due to size (<3 mm) and/or location.5 There is as yet no standard examination method for establishing a diagnosis of sialolithiasis, although a wide variety of imaging procedures are applicable. Plain conventional radiographic examinations, computed tomography (CT), digital subtraction sialography, magnetic resonance (MR) sialography, and ultrasonography have been used with variable degrees of diagnostic success.6-19 Computed tomography, particularly cone-beam CT (CBCT), is today the preferred examination modality, with reported sensitivity and specificity values of up to 98.85%.8,9 The logistics, costs, and radiation exposure involved in the method are inherent limitations and disadvantages, however. Although MR sialography has been used successfully, with sensitivity and specificity rates >90%, it has not become established in routine clinical practice due to its costs and efforts.13,16,17

Ultrasonography is becoming increasingly important as a diagnostic tool in sialolithiasis, with a sensitivity of 77% to 95% and a specificity of 80% to 100%.12,14,15,18-21 Ultrasound is a dynamic real-time method that does not involve radiation exposure and can be carried out cost-effectively by clinicians themselves. Sialendoscopy is now an established method for managing obstructive diseases in the major salivary glands. It has been shown that sialendoscopy can detect stones that are not visualized using other imaging tools.2,22 On the basis of our group’s experience, we would argue that the diagnostic precision of high-resolution B-scan ultrasound can be supplemented with sialendoscopy, making it possible to establish an accurate

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diagnosis in virtually every case of sialolithiasis. The objective of this study was to assess the value of ultrasound supplemented by sialendoscopy and propose this as an alternative standard for diagnosing sialolithiasis.

Methods
This retrospective study was carried out at the Department of Otorhinolaryngology, Head and Neck Surgery of the University of Erlangen–Nuremberg, Germany. Approval for the study was obtained from the local institutional review board of the Friedrich-Alexander University of Erlangen–Nuremberg, and informed consent was obtained from all study participants.

All patients who presented with a suspected diagnosis of obstructive sialopathy between January 2011 and April 2017 were evaluated. To exclude bias, only patients who were presenting in the department for the first time and had not undergone previous treatment elsewhere were considered. A total of 2052 patients and 2277 glands were included in the study. The patients’ mean age was 46.8 ± 16.1 years (range, 1-89 years); 52.4% were women (1076/2052), and 47.6% were men (976/2052).

Clinical criteria for a suspected diagnosis of obstructive sialopathy were periprandial swelling of the salivary glands, recurrent unclear pain in the area of the salivary glands, enlargement of the major salivary glands, and recurrent sialadenitis. All patients underwent an ultrasound examination of the submandibular gland (SMG), sublingual gland (SLG), and parotid gland (PG). The examination was carried out using high-end ultrasound devices (Siemens ACUSON S2000 and S3000; Siemens Medical Solutions USA, Malvern, Pennsylvania). Every patient was examined by at least 2 otolaryngology specialists with several years of experience in ultrasonography and in the treatment of salivary gland diseases. The sonographic examination was routinely recorded. The diagnosis was established by a pretherapeutic ultrasound examination and was not revised retrospectively to exclude any bias. Stimulation of glandular secretion with oral administration of vitamin C was used to enhance the findings in patients with unclear ductal obstruction.

Hyperechoism with distal signal loss in the duct was evaluated as a sign of sialolithiasis. The stones were classified according to their location as intraparenchymal stones, proximal/hilar stones, stones in the middle third, and stones in the distal ductal system, including the papillary region, on the basis of replicable sonographic landmarks, as already described in a previous study.

All patients with signs of obstructive sialopathy—with or without sonographic suspicion of sialolithiasis—underwent sialendoscopy to establish the diagnosis and plan and/or carry out the appropriate therapy. Treatment was performed in accordance with established algorithms, which include interventional sialendoscopy, transoral ductal incision, extracorporeal shock-wave lithotripsy (ESWL), intraductal pneumatic lithotripsy, or a combination of these.

The definitive diagnosis of sialolithiasis, and the reference standard used, was direct visualization of the stone during diagnostic/interventional sialendoscopy. With intraparenchymal stones that could not initially be visualized using sialendoscopy, ESWL was used to disintegrate and/or mobilize the stones. ESWL proved to convert invisible/inaccessible stones into visible/accessible stones. Passage of fragments in the saliva after stone fragmentation and evidence of stones/fragments on follow-up sialendoscopy after ESWL were used as evidence of sialolithiasis defining the true positives. Simultaneous sialendoscopy and ultrasound were used to clarify diagnoses in which false-positive ultrasound findings were suspected or to diagnose and locate stones precisely within the ductal system. This combination of diagnostic methods was very useful for determining whether hyperechoism had an extraductal or extraparenchymal location and/or was present in combination with sialolithiasis.

Statistical analysis was performed using SPSS Statistics for Windows, version 22.0 (SPSS, Inc, an IBM Company, Chicago, Illinois). Data are given as means plus or minus standard deviation, with values for accuracy, sensitivity, specificity, and range, along with the positive predictive value (PPV) and negative predictive value (NPV).

Results
Of the total of 2277 glands (2052 patients) retrospectively investigated, 1307 (57.4%) were SMGs, 966 (42.4%) were PGs, 3 were SLGs (0.1%), and 1 was a heterotopic accessory gland of the parotid gland (Tables 1 and 2).

Ultrasonography raised a suspicion of sialolithiasis in 1320 of the 2277 glands (57.97%; 1023 SMGs, 3 SLGs, and 273 PGs). Using our reference standard, sialolithiasis was diagnosed in 1337 of the 2277 glands (58.72%; 1060 SMGs, 273 PGs, 3 SLGs, and 1 in a heterotopic accessory gland of the parotid gland).

The stones diagnosed with ultrasonography had a mean size of 6.3 ± 3.1 mm (range, 1.8-20.0 mm) in the PG and 7.4 ± 3.8 mm (range, 1.5-37.0) in the SMG.
Anatomic location of sialoliths within the salivary ductal system is shown in Table 2. In submandibular glands, 46% were located in the hilum and 25% in the distal duct. In the parotid glands, this was reversed, with the distal duct followed by the hilum as the most common locations (40% and 27%, respectively).

A total of 68 false-negative findings (50 in the SMG, 17 in the PG, and 1 in the sublingual gland) and 51 false-positive findings were identified for ultrasound (26 in the SMG and 25 in the PG) (Table 3).

Diagnostic test metrics, including accuracy, sensitivity, specificity, PPV, NPV, false-positive rates, and false-negative rates of sonography as a single-mode examination tool, are provided in Table 3.

Sialendoscopy was valuable in particular in cases of unclear, false-positive, or false-negative findings on ultrasound. False-positive and false-negative findings on ultrasound were <4% (Tables 1 and 3). The correct diagnosis was established in all cases by direct stone identification with sialendoscopy or by excluding sialolithiasis by locating a questionable hyperechoic reflex in an extraductal/extraparenchymal site. Deep parenchymal stones initially not visible by sialendoscopy were seen (fragments) in the sialendoscopy following ESWL, demonstrating the original deep parenchymal hyperechoism as a sialolith.

The stones in the SMG that were only discovered on sialendoscopy (false-negative results) were usually small (2.27 ± 0.65 mm; range, 1.5-3.0 mm), soft in consistency, and in 80% of the cases located in the most distal part of the efferent duct (Table 2; Figure 1A, B and Figure 2). Overall, 15.3% (40/261) of stones in the distal part of Wharton’s duct, 6.25% (4/64) of those in the middle third, but only 0.6% (3/492) of those in the proximal part of Wharton’s duct were not detectable on ultrasound (Table 2). In the presence of multiple/multilocular sialolithiasis, stones were not detected in 1.6% of the patients (3/178). Intraparenchymal stones were always detected on ultrasound. Accompanying duct dilation was identified in 94%, and the diameter of the duct was 3.5 ± 1.2 mm (range, 1.4-7.0 mm). Only 6% of the false-negative findings (3/50) showed no signs of ductal congestion.

In the PG, false-negative results were obtained in 1.76%, with the stones being located distally in most cases (52.9%). Of these, 8.1% (9/110) escaped ultrasound detection.

### Table 2. Distribution of Stones in the Various Segments of the Efferent Duct of the Submandibular Gland or Parotid Gland When Sialolithiasis Was Actually Present.

<table>
<thead>
<tr>
<th>Location of Sialolith</th>
<th>Submandibular Gland, No. (%)</th>
<th>Parotid Gland, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>False-Negative Results, n = 50 (100%)</td>
<td>Total Glands with Stones, n = 1060 (100%)</td>
</tr>
<tr>
<td>Distal</td>
<td>40 (80)</td>
<td>261 (25)</td>
</tr>
<tr>
<td>Middle third</td>
<td>4 (8)</td>
<td>64 (6)</td>
</tr>
<tr>
<td>Hilum</td>
<td>3 (6)</td>
<td>492 (46)</td>
</tr>
<tr>
<td>Intraparenchymal</td>
<td>0 (2)</td>
<td>65 (6)</td>
</tr>
<tr>
<td>Several locations</td>
<td>3 (6)</td>
<td>178 (17)</td>
</tr>
</tbody>
</table>

### Table 3. Test Performance Metrics for Ultrasound in Sialolithiasis.

<table>
<thead>
<tr>
<th>Diagnostic Test Performance Metric</th>
<th>Value Overall (95% CI)</th>
<th>Value for Submandibular Gland (95% CI)</th>
<th>Value for Parotid Gland (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>94.9 (93.6-96.0)</td>
<td>95.3 (93.8-96.5)</td>
<td>93.8 (90.2-96.3)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>94.6 (92.9-95.9)</td>
<td>89.5 (85.0-93.0)</td>
<td>96.4 (94.7-97.7)</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>17.49 (13.39-22.85)</td>
<td>9.05 (6.29-13.02)</td>
<td>25.99 (17.67-38.24)</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.054 (0.043-0.068)</td>
<td>0.05 (0.04-0.07)</td>
<td>0.06 (0.04-0.10)</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>96.1 (95.0-97.0)</td>
<td>97.5 (96.4-98.2)</td>
<td>91.1 (87.4-93.8)</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>92.9 (91.2-94.3)</td>
<td>81.6 (77.1-85.3)</td>
<td>97.5 (96.1-98.4)</td>
</tr>
<tr>
<td>Accuracy, %</td>
<td>94.8 (93.8-95.7)</td>
<td>94.2 (92.8-95.4)</td>
<td>95.7 (94.2-96.9)</td>
</tr>
<tr>
<td>False-negative rate, %</td>
<td>5.1 (4-6.4)</td>
<td>4.7 (3.5-6.2)</td>
<td>6.2 (3.7-9.8)</td>
</tr>
<tr>
<td>False-negative findings, %</td>
<td>3.0</td>
<td>3.8</td>
<td>1.8</td>
</tr>
<tr>
<td>False-positive rate, %</td>
<td>5.4 (4.1-7.1)</td>
<td>10.5 (7-15)</td>
<td>3.6 (2.3-5.3)</td>
</tr>
<tr>
<td>False-positive findings, %</td>
<td>2.4</td>
<td>2.0</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
Intraparenchymal stones and multiple/multilocular sialoliths were, however, detectable with ultrasound in all cases (Table 2). Stones that were visualized only with sialendoscopy were 3.0 ± 0.82 mm in size (range, 1.5-4.0 mm). All false-negative findings in the parotid gland showed ductal dilation as sign of obstructive sialopathy (maximum diameter of the congested duct: 2.9 ± 1.4 mm; range, 1.2-6.0 mm).

Analyzing the SMG and PG together showed that most of the stones not detected by ultrasound (73.1%; 40 in SMG and 9 in the PG of 67 false negatives for both glands) were located in the distal part of the duct (Table 2), which is also the part of the ductal system best accessible with the sialendoscope.

One of the 3 sialolithiasis cases of the SLG was a false negative in ultrasound.

With the false-positive findings, the ultrasound diagnosis of sialolithiasis was revised in all cases after sialendoscopy was performed. If sialendoscopy also did not reveal the correct diagnosis concerning an unclear hyperechoism, further radiologic imaging (eg, MR imaging [MRI]) was indicated.

A total of 51 false-positives were identified (25 in the PG and 26 in the SMG). In the PG, 32% (8/25) were extraductal calcifications; 64% (16/25) were related to stenosis (Figure 3A, B and Figure 4A, B), scars, and/or ductal inflammation; and in 1 case (4%, 1/25), the finding was due to air bubbles trapped in Stensen’s duct. In the SMG, 26.9% of the false positives (7/26) were extraductal calcifications; 69.2% (18/26) were caused by stenoses, scars, and/or ductal inflammation; and 3.8% (1/26) were due to air bubbles trapped in Wharton’s duct. In 7 cases, the definitive diagnosis was not clear with ultrasound, and MRI was therefore indicated. These cases proved to be due to phlebolith (SMG, n = 1), vascular malformations (SMG and PG, n = 1), intratendinous calcifications within the mylohyoid muscle (SMG, n = 1) and masseter muscle (PG, n = 1), calcified lymph nodes (PG, n = 1), and a calcified tumor adjacent to the duct (PG, n = 1).

Discussion

These results confirm the excellent diagnostic value of ultrasound in sialolithiasis, with an accuracy, sensitivity, specificity, PPV, and NPV of 94.91%, 94.57%, 96.14%, 92.89%, and 94.77%, respectively (Table 3).

The value of ultrasound has already been examined in various publications, but nearly all of these have only included smaller numbers of cases (<100). Values for sensitivity and specificity in the range of 73% to 77% and 90% to 95%, respectively, have been reported.14,15,18-21 A recent study by our own group demonstrated the value of ultrasound in more than 600 patients, with overall sensitivity and specificity rates of 94.7% and 97.4%, respectively.12

Even in experienced hands, ultrasound examinations are associated with minor inaccuracies, indicated by a false-negative rate and a false-positive rate of, respectively, 5.1% and 5.4%. One of the obstacles with ultrasound in the SMG is the acoustic shadow created by the mandible (Figure 1A, B and Figure 2). In addition, the large distance from transducer to the floor of the mouth, particularly at the

Figure 1. False-negative finding in submandibular gland sialolithiasis: sonography shows a dilated Wharton’s duct (diameter 3.5 mm; A, B). The most distal part of the duct could not be adequately visualized due to the acoustic shadow of the mandible (B).

Figure 2. A small, mobile stone with a size of 1.5 to 2 mm is visualized by sialendoscopy only in the most distal part of the duct near the papilla and removed near the hilum by basket extraction.
ostium, may prevent visualization, particularly of stones located in the distal Wharton’s duct. Competing hyperechoism caused by fibrotic and/or calcified tissue next to the duct or by air on the surface of the mucosa may also be mistaken for sialoliths. Stones in the PG may be overlooked due to competing hyperechoism associated with the complex anatomy along Stensen’s duct. Teeth, hyperechoism caused by changes in impedance at the oral mucosal surface, or even air bubbles may be misdiagnosed as stones, as is the case in intraductal fibrosis (eg, ductal stenosis, Figure 3A, B and Figure 4A, B) or extraductal calcifications. It is therefore not surprising that 73.1% of stones not seen with ultrasound alone were located in the distal duct in both glands (Table 2), which highlights the complementary value of sialendoscopy as this is the most easily accessible area of the duct. The option of using transoral ultrasound may be able to fill this diagnostic gap, but it requires further investigation. Manual palpation of the floor of the mouth can also improve the detection rate of salivary stones not visible by sonography, particularly when these are located at the papilla or in the distal duct as pointed out in a recent article.

In cases of false-negative findings, the stones tended to be smaller in the SMG (mean, 2.27 mm) than in the PG (mean, 3.0 mm). This may be explained by the well-known greater degree of calcification of submandibular stones. Intensive ductal irrigation during sialendoscopy may cause mobilization of small, mobile, and often peripheral located stones. In unclear cases, after a second ultrasound check after sialendoscopy, these stones may be seen intraductally after mobilization to sonographic favorable sites.

In all false-positive cases, the presence of intraductal sialoliths was excluded using sialendoscopy, and hyperechoism adjacent to the duct was better characterized.

Our results indicate that ultrasound examination should be regarded as a key examination and as the method of first choice for diagnosing sialolithiasis of the major salivary glands. Sonography is performed by the examining clinician before the procedure, during the procedure (interventional sialendoscopy, transoral ductal surgery, and/or ESWL) to confirm or exclude unclear sonographic findings, and immediately afterward to reassess the success of treatment and for follow-up. This dynamic examination sequence is highly cost-effective, does not cause any radiation exposure or contrast administration, and can be repeated as often as needed. For these reasons, it is also suitable for sensitive patients such as children or pregnant women.

It has been shown that direct visualization with sialendoscopy provides additional value to other imaging tools. Koch et al investigated over 100 patients with obstructive disease of the major salivary glands that had remained unclear despite various prior imaging procedures, including ultrasound and CT. It was shown that the correct diagnosis of sialolithiasis could be established only by sialendoscopy in 20.8% of these cases. Vashishta and Gillespie identified sialolithiasis as the cause of chronic idiopathic sialadenitis in 8% of cases after performing sialendoscopy. When the ultrasound findings and the sialendoscopy findings were combined, definitive clarification of all false-positive and false-negative findings after the ultrasound examination was possible, and the diagnosis of sialolithiasis could be established or excluded in virtually every case. Sialendoscopy allows direct visualization of the ductal system up to posthilar ducts of the fourth order. In addition, simultaneous treatment for the underlying cause is possible in most cases.

The results achieved with ultrasound examinations alone are comparable with those with the competing imaging
methods. In earlier publications on the sensitivity and specificity of CT, including CBCT, excellent results were reported. Dreiseidler et al reported sensitivity and specificity values as high as 98.85% after examining 29 patients with sialolithiasis (5 PGs, 24 SMGs), as confirmed by surgical removal of the glands as the gold standard in comparison with a control group of healthy individuals/glands. The authors highlighted examiner independence, reproducibility, and relatively low radiation exposure in the diagnosis of sialolithiasis as advantages of this examination method. The data presented here, including a much larger number of patients, are comparable with those obtained with CBCT but have the advantages offered by ultrasound in comparison with all radiologic modalities. Drage and Brown showed that CBCT sialography is at least as good as plain sialography. Digital subtraction sialography alone has been reported to have a sensitivity of 96% to 100% and a specificity of around 90% and is regarded as the gold standard in many studies.

In a study including 123 patients, Kiringoda et al also reported that CT and MRI are able to exclude sialolithiasis in every case, in comparison with sialendoscopy. In small groups of patients not exceeding 25 cases, MR sialography was evaluated by Becker et al, who described sensitivity, specificity, PPV, and NPV rates of 91%, 94% to 97%, 93% to 97%, and 91%, and by Jäger et al, who reported a sensitivity of 80% and a specificity of 100% for MR sialography with 3D constructive interference in steady-state (CISS) imaging. However, the costs, feasibility in clinical practice, potential for artifacts caused by metallic structures in the vicinity (eg, prostheses), and movement artifacts limit the value of MR sialography. In addition, the stones cannot be visualized directly. When sialendoscopy is used, the minor inadequacies of ultrasonography in diagnosing sialolithiasis can be overcome—although ultrasound already shows a diagnostic value comparable to the best results obtained with CT and MRI. In comparison with the competing radiologic methods, they are cost-effective, are not associated with risks and side effects such as radiation exposure, and can be performed using local anesthesia. In addition, both diagnostic tools can be used also by the clinician and are valuable for planning, performing the treatment, and checking the success of therapy during the follow-up.

Because deep parenchymal stones are usually not visible by sialendoscopy, we recommend that sonography should be performed initially in all cases of suspected sialolithiasis, followed by sialendoscopy to definitively assess all other locations within the ductal system. Further embedding of ultrasound and sialendoscopy into a practical oriented diagnostic and therapeutic regimen under specific consideration of the cost-effectiveness may be a focus of future research in this field. Limitation of this study is the retrospective design. On the other hand, prospective studies (eg, compare of ultrasound and sialendoscopy with radiologic examination tools like CT scan) are associated with unfavorable side effects/risks and may cause ethical concerns.

Conclusion
The present results suggest a high diagnostic value of ultrasound for establishing the diagnosis of sialolithiasis. When the findings of ultrasound and sialendoscopy are added, almost every case of sialolithiasis can be adequately assessed. We would therefore propose that ultrasound and sialendoscopy are candidates for use as standard investigation tools in the diagnosis of sialolithiasis. The 2 examination methods represent a substantial part of the armamentarium in our own as in many other units dealing with salivary gland diseases.

Author Contributions
Michael Koch, substantial contributions to the conception and design of the work; the acquisition, analysis, interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved;
Miguel Goncalves, substantial contributions to the conception and design of the work; the acquisition, analysis, interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved;
Konstantin Mantzopoulos, data analysis, revising it critically for important intellectual content, final approval of the version to be published, accountability for the work; Mirco Schapher, data analysis, revising it critically for important intellectual content, final approval of the version to be published, accountability for the work; Heinrich Iro, data analysis, revising it critically for important intellectual content, final approval of the version to be published, accountability for the work.

Disclosures
Competing interests: None.
Sponsorships: None.
Funding source: None.

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