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Review Article

Application of sialography in diagnosis and differential diagnosis of igg4-related sialadenitis. A systematic review.

Dr. Dharmapuri Govindhan Dharani Dharan[1], Dr. Karthik Shunmugavelu[2*] , Vidharshana[3].
[1]Private practice, Mediscan systems No 197 , dr natesan road Mylapore chennai 600004 Tamilnadu India
[2]Assistant Professor, Department of Dentistry, PSP medical college hospital and research institute Tambaram Kanchipuram main road Oragadam Panruti Kanchipuram district Tamilnadu 631604 India.
[3]Undergraduate (MBBS). PSP medical college hospital and research institute Tambaram Kanchipuram main road Oragadam Panruti Kanchipuram district Tamilnadu 631604 India.

Abstract

Background:
Immunoglobulin G4-related disease (IgG4-RD) is a systemic fibroinflammatory condition frequently involving salivary glands. IgG4-related sialadenitis often mimics neoplastic and other inflammatory disorders, creating diagnostic difficulty. Sialography provides detailed visualization of salivary ductal architecture and may aid in differentiation.

Methodology:
A systematic review was conducted using PubMed, Scopus, Embase, Web of Science, and LILACS databases for studies published between 2020 and 2024. Original research articles focusing on imaging or diagnosis of IgG4-related sialadenitis were included. Study selection and data extraction were performed independently by two reviewers. Extracted variables included study design, sample size, imaging modality, and diagnostic findings. Study quality was assessed using STROBE criteria. Due to heterogeneity, a narrative synthesis was undertaken.

Results:
A total of 11 studies met the inclusion criteria. Sialography demonstrated characteristic ductal changes such as ductal irregularities, segmental narrowing, and sialectasis. These features were useful in differentiating IgG4-related sialadenitis from conditions such as Sjögren's syndrome and obstructive sialadenitis. Diagnostic accuracy improved when sialography was combined with other imaging modalities including ultrasound, CT, and MRI. Evidence quality was low to moderate due to observational study designs and heterogeneity.

Conclusion:
Sialography serves as a valuable adjunctive imaging modality for evaluating ductal morphology in IgG4-related sialadenitis. However, it is not sufficient as a standalone diagnostic tool and should be interpreted alongside clinical, serological, and histopathological findings.

Recommendation:
A multimodal diagnostic approach integrating imaging, serology, and histopathology is recommended for accurate diagnosis. Future studies with standardized imaging protocols and larger sample sizes are required to establish the definitive diagnostic role of sialography.

***Keywords**: Salivary glands; IgG4-related sialadenitis; Chronic obstructive submandibular sialadenitis; Differential diagnosis, Ultrasound, Sialography, Benign salivary gland obstruction*
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***Corresponding Author:** Dr. Karthik Shunmugavelu*
*Email: **drkarthiks1981@gmail.com***
https://orcid.org/0000-0001-7562-8802
Assistant Professor, Department of Dentistry, PSP medical college hospital and research institute Tambaram Kanchipuram main road Oragadam Panruti Kanchipuram district Tamilnadu 631604 India

Introduction

Salivary glands were the primary organs of digestion to release digestive fluids into the oral cavity. The principal paired salivary glands are the parotid, submandibular, and sublingual glands, in decreasing size order. In addition, there are several small minor salivary glands randomly dispersed throughout the upper aerodigestive tract, including the paranasal sinuses and parapharyngeal regions. The images are focused on the primary salivary glands. Plain radiography and standard sialography are

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two widely used imaging techniques. High-resolution ultrasonography (HRUS) has recently gained popularity for focused salivary gland imaging. Sialadenitis is the most frequent disease of the salivary glands. Patients exhibit xerostomia, discomfort, and an unpleasant taste in their mouths in addition to salivary gland enlargement. Acute, chronic, or acute on top of chronic presentations are all possible. Immunoglobulin G4-related sialadenitis (IgG4-RS), granulomatous, lympho-epithelial, acute or chronic infectious, obstructive, and post-treatment sialadenitis are among the causes of sialadenitis. Elevated serum IgG4 levels, tissue infiltration with lymphocytes, fibrosis, and consequent organ dysfunction are the hallmarks of immunoglobulin G4-related disease (IgG4-RD), a systemic immune-mediated illness. In 2003, IgG4-RD was originally identified as a disease entity when several previously unrelated illnesses were found to coexist in some individuals. It is now known that these disorders are a component of IgG4-RD. Since its initial description, IgG4-RD has been demonstrated to impact almost every organ in the body, with the salivary glands being among the most affected. IgG4-RD prefers specific organ systems, but it can damage any organ. The most damaged organs include the digestive system and hepatic duct, the respiratory system, the urinary tract, the cardiovascular system and the peritoneum, the meninges, the thyroid, the orbits, the lacrimal glands, and the major salivary glands. The illness usually progresses in two stages, with an initial inflammatory phase and a fibrosing result. This systematic review aims to evaluate the diagnostic utility of sialography in IgG4-related sialadenitis and its role in differentiating it from other salivary gland pathologies.

Material and methods:

Eligibility Criteria

Original research articles (2020–2024), English language, focusing on IgG4-related sialadenitis and imaging. Reviews, editorials, and irrelevant studies excluded.

Information Sources

Databases searched: PubMed, Scopus, Embase, Web of Science, LILACS.
Last search date: March 2026.

Search Strategy

Keywords: ("IgG4") AND ("sialadenitis" OR "salivary gland") AND ("sialography" OR "imaging" OR "differential diagnosis").

Selection Process

Two independent reviewers screened titles/abstracts and full texts. Disagreements resolved through discussion. No automation tools used.

Data Collection Process

Data extracted independently by two reviewers. Cross-verification performed. No author contact required.

Data Items

Author, year, country, study design, sample size, imaging modality, diagnostic findings.

Study Risk of Bias Assessment

Assessed using STROBE checklist independently by two reviewers.

Effect Measures

Descriptive outcomes (diagnostic findings, imaging characteristics).

Synthesis Methods

Grouped by imaging modality and diagnostic findings

Narrative synthesis performed (no meta-analysis due to heterogeneity)

Reporting Bias Assessment

Not performed due to limited number of studies.

Certainty Assessment

Not performed; insufficient quantitative data.

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Results:

Study Selection

Records identified: 78
Screened: 78
Excluded: 67
Included: 11

Study Characteristics

Include: study design, country, sample size, imaging modality.

Risk of Bias

Most studies observational with moderate quality (STROBE compliance).

Results of Synthesis

Sialography shows ductal irregularities, sialectasis. Helps differentiate IgG4-RS vs Sjögren's syndrome. Works best when combined with US/CT/MRI

Heterogeneity

Not assessed quantitatively.

Sensitivity Analysis

Not performed.

Reporting Bias

Not assessed.

Certainty of Evidence

Low to moderate (observational data).

Table 1 – An overview

Author	Title	Journal	Outcome
Samar Aboulenain, Tatiana P Miquel, Juan J Maya	Immunoglobulin G4 (IgG4)-Related Sialadenitis and Dacryoadenitis With Chronic Rhinosinusitis	Aboulenain S, Miquel TP, Maya JJ. Immunoglobulin G4 (IgG4)-related sialadenitis and dacryoadenitis with chronic rhinosinusitis. Cureus. 2020 Aug 15;12(8). doi: 10.7759/cureus. 9756.	IgG-related disease is a new entity that can be a rare etiology, diagnosis should be based on clinical, serological, and pathological findings.
Elin Peuraharju, Jaana Hagström, Jussi Tarkkanen, Caj Haglund & Timo Atula	IgG4-positive plasma cells in nonspecific sialadenitis and sialolithiasis	Peuraharju E, Hagström J, Tarkkanen J, Haglund C, Atula T. IgG4-positive plasma cells in nonspecific sialadenitis and sialolithiasis. Modern Pathology. 2022 Oct;35(10):1423-30. doi.org/10.1038/s413 79-022-01089-5	IgG4-positive inflammatory infiltrates represent a part of a continuous inflammatory process most likely a phenomenon distinct from genuine IgG4-related disease
Sushama Govindrao Gurwale, Charusheela Rajesh Gore, Ishita Gulati, Indranil Dey	Immunoglobulin G4-related chronic sclerosing sialadenitis: An emerging entity	Gurwale SG, Gore CR, Gulati I, Dey I. Immunoglobulin G4-related chronic sclerosing sialadenitis: An emerging entity. Journal of Oral and Maxillofacial Pathology. 2020 Feb 1;24(Suppl 1):S135-8.doi: 10.4103/jomfp. JOMFP_83_17	Immunohistochemistry for IgG4 is helpful to clinch the diagnosis.
W-X Zhu, Y-Y Zhang, Z-P Sun, Y Gao, Y Chen, G-Y Yu	Differential diagnosis of immunoglobulin G4-related sialadenitis and Kimura's disease of the	Zhu WX, Zhang YY, Sun ZP, Gao Y, Chen Y, Yu GY. Differential diagnosis of immunoglobulin G4-related	Comprehensive evaluation of clinical, serological, radiological, and histopathological

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	salivary gland: a comparative case series	sialadenitis and Kimura's disease of the salivary gland: a comparative case series. International journal of oral and maxillofacial surgery. 2021 Jul 1;50(7):895-905.doi: 10.1016/j.ijom.2020.05.023.	features is crucial for the differential diagnosis
Abigail E. Moore, Kathryn S. Marcus, Anand Rajan KD, Joan E. Maley and Henry T. Hoffman,	Ultrasound and Sialogram Correlates to Parotid Immunoglobulin G4-Related Disease	Moore AE, Marcus KS, Rajan KD A, Maley JE, Hoffman HT. Ultrasound and sialogram correlates to parotid immunoglobulin g4-related disease. Ear, Nose & Throat Journal. 2024 May;103(5):NP247-51.doi: 10.1177/0145561321 1051651.	parotid sialographic and sonographic analogs of histopathologically proven IgG4-RD of the submandibular salivary glands
Agata Czarnywojtek, Abbas Agaimy, Krzysztof Pietrończyk, Iain J. Nixon, Vincent Vander Poorten, Antti A. Mäkitie, Mark Zafereo, Ewa Florek, Nadia Sawicka-Gutaj, Marek Ruchała & Alfio Ferlito	IgG4-related disease: an update on pathology and diagnostic criteria with a focus on salivary gland manifestations	Czarnywojtek A, Agaimy A, Pietrończyk K, Nixon IJ, Vander Poorten V, Mäkitie AA, Zafereo M, Florek E, Sawicka-Gutaj N, Ruchała M, Ferlito A. IgG4-related disease: an update on pathology and diagnostic criteria with a focus on salivary gland manifestations. Virchows Archiv. 2024 Mar;484(3):381-99.doi: 10.1007/s00428-024-03757-0.	Immunoglobulin G4-related disease is a multi-organ disorder characterized by a highly variable clinical presentation
Mingzhu Zhou, Yanying Liu, Shanshan Zhang, Xiaoyan Xie, Wei Li, Li Cui, Hanxue Zhao, Sumei Tang, Xiangdong Hu, Shanshan Wu, Jiajing Peng, Huilian Huang, Wei Ren, Ying Zhang, Ning Xu, Pengfei Sun, Yiqun Liu, Zuyan Zhang, Guangyan Yu, Yin Su	Diagnostic value of a novel salivary gland ultrasound scoring system in IgG4-related sialadenitis	Zhou M, Liu Y, Zhang S, Xie X, Li W, Cui L, Zhao H, Tang S, Hu X, Wu S, Peng J. Diagnostic value of a novel salivary gland ultrasound scoring system in IgG4-related sialadenitis. Rheumatology. 2025 Feb;64(2):747-55.doi: 10.1093/rheumatology /keae121.	A novel semiquantitative ultrasound scoring system for patients with IgG4-RS has good diagnostic performance
Diane Mar, Robert M Fairchild	Imaging of the Major Salivary Glands in Rheumatic Disease	Mar D, Fairchild RM. Imaging of the Major Salivary Glands in Rheumatic Disease. Rheumatic Disease Clinics. 2024 Nov 1;50(4):701-20.doi: 10.1016/j.rdc.2024.07.008.	Salivary gland involvement is a common feature of rheumatologic disease
Reema Mahmoud, Clariel Ianculovici, Shlomi Kleinman & Oren Peleg	IgG4-related sialadenitis — a rare bilateral	Mahmoud R, Ianculovici C, Kleinman S, Peleg O. IgG4-related sialadenitis—a rare	bilateral submandibular salivary gland swelling

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	submandibular gland enlargement: case report	bilateral submandibular gland enlargement: case report. Oral and Maxillofacial Surgery. 2022 Dec;26(4):673-7.doi: 10.1007/s10006-021-01020-3.	with a diagnosed of IgG4-RS
Y Liu, Z Wang, L Ren, Q Zeng, Z Wang , W Bian, Y Zhang, J Fu, D Chen, G Yu, S Zhang, Z Li1	Sonographic findings of immunoglobulin G4-related sialadenitis and differences from Sjögren's syndrome	Liu Y, Wang Z, Ren L, Zeng Q, Wang Z, Bian W, Zhang Y, Fu J, Chen D, Yu G, Zhang S. Sonographic findings of immunoglobulin G4-related sialadenitis and differences from Sjögren's syndrome. Scandinavian Journal of Rheumatology. 2022 Mar 4;51(2):128-34.doi: 10.1080/03009742.2021.1917144.	Scored sonographic features were helpful in differentiating IgG4-RS from SS
Hiroto Tsuboi, Fumika Honda, Hiroyuki Takahashi, Yuko Ono, Saori Abe, Yuya Kondo, Isao Matsumoto, Takayuki Sumida	Pathogenesis of IgG4-related disease. Comparison with Sjögren's syndrome	Tsuboi H, Honda F, Takahashi H, Ono Y, Abe S, Kondo Y, Matsumoto I, Sumida T. Pathogenesis of IgG4-related disease. Comparison with Sjögren's syndrome. Modern rheumatology. 2020 Jan 2;30(1):7-16.doi: 10.1080/14397595.2019.1650694.	Potentially used fo identification of disease specific biomarkers an development of therapie for IgG4-RD

Discussion

Key Findings

The present systematic review identified that sialography consistently demonstrates ductal abnormalities in IgG4-related sialadenitis (IgG4-RS), including irregular ductal dilatation, segmental narrowing, and sialectasis (52,57). These features are clinically relevant in differentiating IgG4-RS from other salivary gland disorders. In particular, obstructive sialadenitis typically presents with localized ductal dilatation associated with calculi or strictures (54,60), whereas Sjögren's syndrome exhibits punctate or globular sialectasis with progressive glandular destruction (57,66). In contrast, IgG4-RS often shows relatively uniform ductal involvement with preserved architecture despite gland enlargement (67).

Interpretation

The findings indicate that sialography functions primarily as a complementary diagnostic modality rather than a standalone tool. Although it provides detailed visualization of ductal anatomy, definitive diagnosis of IgG4-RS still depends on integration with clinical features, serological markers such as elevated serum IgG4, and histopathological confirmation (7,39,40). Imaging findings alone are insufficient due to overlap with inflammatory and neoplastic conditions, including lymphoma and Sjögren's syndrome (43,72).

Comparison with Literature

The observations from this review are consistent with prior imaging-based studies demonstrating that diagnostic accuracy improves when multiple imaging modalities are combined. Ultrasonography contributes to the assessment of parenchymal echotexture, while CT and MRI provide information on glandular enlargement and enhancement patterns (63,70,71). However, sialography offers superior delineation of ductal morphology, particularly in second- and third-order branches, which are not consistently visualized with other techniques (59). This complementary role has been emphasized in studies comparing sialography, ultrasound, and sialoendoscopy in salivary gland disorders (65).

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Explanation

The diagnostic value of sialography lies in its duct-centric approach, allowing direct visualization of structural alterations within the salivary ductal system. This provides a distinct advantage over ultrasound, which primarily evaluates parenchymal changes rather than detailed ductal architecture. As IgG4-RS involves inflammatory and fibrotic changes that affect ductal morphology, sialography enables identification of these alterations with greater precision (52,59). This structural assessment is particularly useful in distinguishing diffuse inflammatory conditions from focal obstructive or neoplastic processes.

Generalizability

The applicability of these findings extends to clinical settings where advanced imaging modalities such as MRI sialography may not be readily available. Conventional sialography remains a cost-effective and accessible technique capable of providing detailed ductal information (59,64). This is particularly relevant in resource-limited environments, where reliance on widely available diagnostic tools is necessary.

Limitations

Several limitations are evident in both the included studies and the review process. The sample sizes of the included studies were relatively small, limiting statistical robustness. Considerable heterogeneity was observed in study design, imaging protocols, and diagnostic criteria. There is currently no standardized classification system for interpreting sialographic findings in IgG4-RS, which restricts comparability across studies. Quantitative synthesis was not feasible, and meta-analysis was not performed due to variability in reported outcomes. In addition, potential selection bias cannot be excluded, as the review included only studies published between 2020 and 2024 and restricted to specific databases.

Implications

The findings support the use of a combined diagnostic approach incorporating clinical evaluation, serological testing, imaging, and histopathology (7,34). Sialography should be considered an adjunctive tool that enhances diagnostic confidence when used alongside other modalities. There is a need to develop standardized imaging protocols and reporting criteria for sialography in IgG4-RS to improve reproducibility and diagnostic consistency. Future research should focus on well-designed prospective studies with larger sample sizes to validate the diagnostic utility of sialography and to establish evidence-based imaging guidelines.

Table 2: Clinical phenotypes of IgG4-RD[50]

	Group I, Pancreato-hepatobiliary	Group II, Retroperitoneum/ Aorta	Group III, Head and Neck Limited	Group IV, Mikulicz/Systemic
organ involvement	Pancreas, liver, biliary tree	Retroperitoneum, aorta	Orbit, lacrimal glands, salivary glands, sinuses	Lacrimal glands, salivary glands, sinuses, pancreas, biliary tree, kidneys, lungs, lymph nodes, prostate
Age	Older	Older	Younger	Older
Serum IgG4	Elevated	Normal to mildly elevated	Elevated	Profoundly elevated

Table 3: Imaging findings of sialadenitis[67]

Causes	Imaging findings
Acute bacterial sialadenitis	–Diffuse homogenous enlargement (early) and abscess (late).
Acute viral sialadenitis	–Bilateral diffuse enlargement of parotid glands in children.
Chronic adult sialadenitis	–Irregularly enlarged main duct and central ductal dilatation.

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juvenile recurrent parotitis	–Sialography shows punctate sialectasis with no evidence of obstruction.
Ig G4-related sialadenitis	–Bilateral symmetric enlargement of salivary gland with homogenous pattern and enhancement.
Sjögren's sialadenitis	–Diffusely enlarged homogenous (early), enlarged with multiple cystic regions (intermediate), atrophic with hypoechoic regions (late).
Tuberculous	–Diffuse enlarged glands with abscess and enlarged intra-parotid lymph nodes.
Cat scratch disease	–Enlarged intra-parotid lymph node in children, self-limited disorder.
Sialadenosis	–Bilateral enlarged parotid glands in alcoholics, diabetics and malnourished.

Conclusion

Major salivary gland ducts are evaluated by standard and digital sialography, ultrasound (US), CT imaging, and MR sialography (MR-Si). Conventional sialography is the gold standard method for visualizing the major submandibular gland duct and its interconnected branches. Nevertheless, sialographic testing is an invasive procedure that exposes patients to ionizing radiation and requires the use of an iodinated contrast agent. It should not be used if you have a current illness, thyroid gland condition, or an iodine allergy. Diseases associated with immunoglobulin G4 (IgG4) commonly involve the submandibular gland and occur at sites in the head and neck. Over the past 10 years, a particular type of submandibular sialadenitis—also referred to as chronic sclerosing sialadenitis or a Kuttner tumor—has frequently been thought of as an IgG4-related submandibular gland disease. The gold standard for diagnosing IgG4-related diseases is still histology, and while a conclusive diagnosis is rarely made without a biopsy, the diagnosis is frequently suspected based on clinical and serologic characteristics. This paradigm is unlikely to alter, mainly because the illness resembles neoplastic illnesses and, in many cases, it is nearly impossible to rule out a malignant process without a biopsy, with the help of imaging modalities.

Registration and Protocol

This review was not registered.

Funding

No funding received.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability

Data available within the article.

Author Contributions

- Conceptualization: Karthik Shunmugavelu
- Data collection: Dharanidharan, Vidharshana
- Analysis: All authors
- Manuscript preparation: All authors

List of Abbreviations

- IgG4-RD – Immunoglobulin G4-related disease
- IgG4-RS – IgG4-related sialadenitis
- CT – Computed Tomography
- MRI – Magnetic Resonance Imaging
- US – Ultrasound

Authors Biography

Dr. Dharmapuri Govindhan dharani dharan

Dr. D. G. Dharanidharan is a dental practitioner based in Chennai, India, associated with Mediscan Systems. His clinical work focuses on diagnostic oral pathology and salivary gland disorders. His research interests include imaging-based diagnosis and clinicopathological correlation in oral diseases.
Dr. Karthik Shunmugavelu

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Dr. Karthik Shunmugavelu is an Assistant Professor in the Department of Dentistry at PSP Medical College Hospital and Research Institute, Tamil Nadu, India. He specializes in Oral and Maxillofacial Pathology with international academic affiliations. His research focuses on oral potentially malignant disorders, biomarkers, and advanced diagnostic techniques.

Vidharshana

Vidharshana is an undergraduate medical student (MBBS) at PSP Medical College Hospital and Research Institute, Tamil Nadu, India. She has an academic interest in systemic diseases with oral manifestations and diagnostic imaging. Her work includes participation in clinical research and systematic reviews.

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