

RUAN SOARES DA SILVA

**ACURÁCIA DIAGNÓSTICA DA ULTRASSONOGRAFIA NA
AVALIAÇÃO DE DOENÇAS INFLAMATÓRIAS E OBSTRUTIVAS DAS
GLÂNDULAS SALIVARES MAIORES: *UMA REVISÃO SISTEMÁTICA
E META-ANÁLISE***

**Faculdade de Odontologia
Universidade Federal de Minas Gerais
Belo Horizonte
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Ruan Soares da Silva

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Monografia apresentada ao Curso de especialização em Radiologia Odontológica e Imaginologia da Faculdade de Odontologia da Universidade Federal de Minas Gerais, como requisito parcial à obtenção do Título de Especialista em Radiologia Odontológica e Imaginologia.

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Ata da Comissão Examinadora para julgamento de Monografia de **RUAN SOARES DA SILVA**, do Curso de Especialização em Radiologia Odontológica e Imagiologia, realizado no período de 02/03/2020 a 31/05/2022.

Aos 31 (trinta e um) dias do mês de maio de 2022, às horas 18 horas, por meio da Plataforma Zoom, reuniu-se a Comissão Examinadora, composta pelos professores Maurício Augusto Aquino de Castro (orientador), Cláudia Borges Brasileiro e Sâmila Gonçalves Barra. Em sessão pública foram iniciados os trabalhos relativos à Apresentação da Monografia intitulada **“ACURÁCIA DIAGNÓSTICA DA ULTRASSONOGRAFIA NA AVALIAÇÃO DE DOENÇAS INFLAMATÓRIAS E OBSTRUTIVAS DAS GLÂNDULAS SALIVARES MAIORES - UMA REVISÃO SISTEMÁTICA E META-ANÁLISE”**. Terminadas as arguições, passou-se à apuração final. A nota obtida pelo aluno foi 100 (Cem) pontos, e a Comissão Examinadora decidiu pela sua aprovação. Para constar, eu, Maurício Augusto Aquino de Castro, Presidente da Comissão, lavrei a presente ata que assino eletronicamente com os outros membros da Comissão Examinadora. Belo Horizonte, 12 de maio de 2022.

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“Se aprendesse qualquer coisa, necessitaria aprender mais, e nunca ficaria
satisfeito.”

Graciliano Ramos, *Vidas Secas*; 1938.

RESUMO

Os distúrbios inflamatórios e obstrutivos das glândulas salivares maiores são muito comuns e podem estar inter-relacionados. A sialadenite é um termo genérico que se refere às alterações inflamatórias e pode ter causa infecciosa, de origem bacteriana ou viral, não infecciosa ou, ainda, por obstrução. A sialolitíase, uma das causas de distúrbios obstrutivos, se dá pela formação de estruturas calcificadas no interior dos parênquimas ou ductos, em decorrência da deposição de sais de cálcio ao redor de debris, notadamente na luz dos ductos. Como ferramenta para o diagnóstico dessas alterações, pode-se lançar mão da ultrassonografia, método seguro, sem efeito deletério conhecido, de custo reduzido, fácil execução e que permite a aquisição de imagens em tempo real, com boa resolução. A presente revisão sistemática e meta-análise teve como objetivo analisar estudos que realizaram avaliação comparativa da acurácia diagnóstica da ultrassonografia para o diagnóstico de sialadenites e sialolitíase, comparativamente a outros métodos de diagnóstico por imagem. Foi realizada busca nas bases de dados eletrônicas PubMed (National Library of Medicine), Web of Science (Thomson Reuters), EMBASE (Elsevier) e SCOPUS (Elsevier), que resultaram na seleção de 1.205 referências. A amostra final foi composta por 10 artigos que contemplaram os critérios de elegibilidade. Foram coletados dados sobre os autores, data de publicação, tipo de estudo, alteração ou patologia avaliada, glândula avaliada e valor diagnóstico da US (ultrassonografia), considerando sua acurácia, sensibilidade, especificidade, valor preditivo positivo, valor preditivo negativo, razão de verossimilhança positiva e razão de verossimilhança negativa. A ultrassonografia apresentou resultados satisfatórios para o diagnóstico das alterações inflamatórias e obstrutivas das glândulas salivares maiores que, comparativamente a outros exames diagnósticos por imagem, a habilitam como um método de escolha para este propósito.

Palavras-chave: Sialolitíase. Sialadenite. Ultrassonografia. Diagnóstico por imagem. Glândulas salivares.

ABSTRACT

Diagnostic accuracy of ultrasonography in the assessment of inflammatory and obstructive diseases of the major salivary glands - A systematic review and meta-analysis

Inflammatory and obstructive disorders of the major salivary glands are very common and may be interrelated. Sialadenitis is a generic term that refers to inflammatory changes in these glands and may have an infectious, bacterial or viral origin, non-infectious or even obstruction. Sialolithiasis, one of the causes of obstructive disorders, is caused by the formation of calcified structures within the parenchyma or ducts of the salivary glands, as a result of the deposition of calcium salts around debris, notably in the lumen of the ducts. As a tool for the diagnosis of these alterations, ultrasound can be used, a safe method, which does not emit ionizing radiation, has no known deleterious effect, is inexpensive, easy to perform and which allows the acquisition of images in real time, with good resolution. Given these assumptions, the present systematic review and meta-analysis aimed to analyze studies that performed a comparative evaluation of the diagnostic accuracy of ultrasound for the diagnosis of sialadenitis and sialolithiasis, compared to other diagnostic imaging methods. A search was performed in the electronic databases PubMed (National Library of Medicine), Web of Science (Thomson Reuters), EMBASE (Elsevier) and SCOPUS (Elsevier), which resulted in the selection of 1,205 references. After reading titles and abstracts, 205 studies remained. These, read in full, led to 10 articles that met the eligibility criteria. Data on authors, date of publication, type of study, alteration or pathology evaluated, gland evaluated and diagnostic value of US (ultrasonography), considering its accuracy, sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and of negative likelihood. Ultrasonography showed satisfactory results for the diagnosis of inflammatory and obstructive changes in the major salivary glands, which, compared to other diagnostic imaging tests, make it a method of choice for this purpose.

Keywords: Sialolithiasis. Sialadenitis. Ultrasonography. Diagnostic Imaging. Salivary Glands.

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LISTA DE ABREVIATURAS E SIGLAS

CT	Tomografia computadorizada / <i>Computed tomography</i>
CBCT	Tomografia computadorizada de feixe cônico / <i>Cone beam computed tomography</i>
MSG	<i>Major Salivary Glands</i>
PROSPERO	Registro Internacional de Revisões Sistemáticas <i>International prospective register of systematic reviews</i>
PRISMA	Principais Itens para Relatar Revisões Sistemáticas e Meta-análises - <i>Preferred Report Items for Systematic Reviews and Meta-Analysis International</i>
QUADAS-2	Avaliação da Qualidade dos Estudos de Precisão Diagnóstica / <i>Quality Assessment of Diagnostic Accuracy Studies</i>
MRI	<i>Magnetic Resonance Imaging</i>
NPV	<i>Negative Predictive Value</i>
PPV	<i>Positive Predictive Value</i>
US	Ultrassonografia / <i>Ultrasonography, ultrasound</i>
RM	Ressonância Magnética
VPN	Valor Preditivo Negativo
VPP	Valor preditivo Positivo

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1 INTRODUÇÃO

Tem-se que 82,9% do total de alterações das glândulas salivares maiores (GSM) são benignas, sendo majoritariamente sialadenites e sialolitíase. A prevalência de condições patológicas, distúrbios inflamatórios e obstrutivos das GSM varia entre 3% e 6% de todas as alterações de cabeça e pescoço (AKIN *et al.*, 1991; PNIAK *et al.*, 2016).

Para aprimorar o processo de diagnóstico por imagem na Odontologia, ferramentas e métodos são constantemente desenvolvidos, visando a obtenção de mais informações, com maior qualidade. Alguns métodos não invasivos possibilitam o diagnóstico diferencial de determinadas patologias e contribuem para o planejamento mais adequado da conduta terapêutica, os quais conseqüentemente levam a um melhor prognóstico, redução da necessidade de reintervenções, maior qualidade de vida e redução de custos aos pacientes (THOMAS; DOUGLAS; RASSEKH, 2017).

Não há apenas uma modalidade de exame por imagem para auxiliar no procedimento de imagem diagnósticos aplicáveis, como radiografia panorâmica, ultrassonografia (US), sialoendoscopia, sialografia com contraste iodado, tomografia computadorizada de feixe cônico (TCFC) e ressonância magnética (RM). Em determinadas situações, mais de um método pode ser aplicado (GONÇALVES *et al.*, 2017; GONÇALVES *et al.*, 2018; GRITZMANN, 1989; ISTEMIHHAN *et al.*, 1991; SCHWARZ *et al.*, 2015;).

Exceto para a US e RM, os demais métodos requerem exposição aos raios X ou são invasivos. Devido ao excelente delineamento do sistema ductal, JÄGER e colaboradores (2000), consideram a sialografia radiográfica como padrão de referência para avaliar sialolitíase das GSM. Thomas e colaboradores (2017), lembram que a TCFC apresenta como desvantagem a aplicação de radiação ionizante, ao passo que apresenta alta sensibilidade e especificidade para o diagnóstico de sialolitíase, além de ser capaz de detectar neoplasias ou abscessos.

Como método diagnóstico útil no processo de investigação de alterações e patologias que afetam as GSM, pode-se lançar mão da US, por se tratar de um método seguro, não emissor de radiação ionizante, que possibilita a visualização dos tecidos moles da região orofacial em imagens com boa resolução, em tempo real, com ampla disponibilidade e custo reduzido. No entanto, o uso da US é altamente dependente de

um operador experiente. (ISTEMIHAN *et al.*, 1991; JÄGER *et al.*, 2000; NG *et al.*, 2017; TERRAZ *et al.*, 2013; THOMAS; DOUGLAS; RASSEKH, 2017).

Diante desta nova perspectiva, a presente revisão sistemática e meta-análise se propôs a selecionar e analisar estudos que avaliaram a acurácia diagnóstica da US comparativamente a outros métodos de exame por imagem, para o diagnóstico de sialadenite e sialolitíase.

2 OBJETIVOS

2.1 Objetivo Principal

Avaliar a acurácia diagnóstica da ultrassonografia para o diagnóstico de sialadenites e sialolitíase, comparativamente a outros métodos diagnósticos por imagem.

2.2 Objetivos Específicos

Comparar a sensibilidade, a especificidade, o valor preditivo positivo e o valor preditivo negativo da ultrassonografia para o diagnóstico de sialadenites e sialolitíase, em relação aos outros métodos de diagnóstico por imagem.

3 RESULTADOS

Os resultados do estudo foram descritos na forma de artigo, escrito na língua inglesa, para ser submetido ao periódico *European Journal of Radiology* (Qualis A1, Fator de impacto: 3528 em 2022).

3.1 Artigo

TITLE: Diagnostic accuracy of ultrasonography in the assessment of inflammatory and obstructive diseases of the major salivary glands - A systematic review and meta-analysis

KEYWORDS: Salivary Gland Calculi, Sialadenitis, Ultrasonography, Diagnostic Imaging, Salivary Glands

1 INTRODUCTION

It is estimated that 82,9% of the total alterations of the major salivary glands (MSG) are benign, mostly sialadenitis and sialolithiasis. The prevalence of pathological conditions, as well inflammatory and obstructive disorders of the MSG, ranges between 3% and 6% of all pathological conditions of head and neck.^{1,2}

In order to improve the diagnostic imaging process in dentistry, tools are continually developed for providing more information with higher quality. Some non-invasive methods allow the differential diagnosis of certain pathologies and contribute to adequate planning of the therapeutic approach, reduction of the need for reinterventions, better quality of life and cost reduction.³

There is no just standard test method to establish the diagnosis of sialadenitis and sialolithiasis, there is a wide variety of diagnostic imaging procedures, such as panoramic radiography (US), endoscopy, iodinated contrast sialography, ultraconic (CBCT) and magnetic resonance imaging (MRI), in some situations more than one method can be applied.^{1,4-7}

Except for US and MRI, others diagnostic imaging methods require exposure to X-rays or are invasive. Due to its excellent delineation of the ductal system, some authors⁸, for example, consider radiographic sialography the standard reference to

assess sialolithiasis in GSM. CBCT has the disadvantage of applying ionizing radiation, while it has high sensitivity and specificity for the diagnosis of sialolithiasis, in addition to being able to detect neoplasms or abscesses.³

As an useful diagnostic method in the investigation of alterations and pathologies that affect MSG, the US can be used due to it is a safe method, which does not emit ionizing radiation, allows the visualization of the soft tissues of the orofacial region with good resolution images, in real time, with low cost. However, the use of ultrasound is highly operator dependent.^{1,3,9-10}

In view of this new perspective, the present systematic review and meta-analysis evaluated the diagnostic accuracy of US, compared to other imaging methods, for the diagnosis of sialadenitis and sialolithiasis.

2 MATERIALS AND METHODS

This systematic review and meta-analysis were reported according to the Preferred Report Items for Systematic Reviews and Meta-Analysis (PRISMA).¹¹ A protocol was registered in the International prospective register of systematic reviews (PROSPERO). The registration number CRD42021295 291 was assigned to the protocol.

2.1 ELIGIBILITY CRITERIA

Original studies of accuracy that compare ultrasonography to other imaging methods for the diagnosis of inflammatory and obstructive disorders of the MSG were eligible for inclusion in this systematic review and meta-analysis. The following PIRD question has been applied: P (patients) = individual; I (index test) = ultrasound; R (reference test) = other imaging method of diagnosis; D (diagnosis) = inflammatory and obstructive disorders of the MSG.

Abstracts of meetings, editorials, qualitative studies, and letters to the editor were excluded. No restrictions on language or publication dates were imposed.

2.2 INFORMATION OF SEARCH STRATEGY

In August/2020, computerized searches were performed in the following electronic databases: PubMed (National Library of Medicine), Web of Science (Clarivate Analytics), EMBASE (Elsevier) and Scopus (Elsevier).

The following specific search strategies were developed:

Ultrasound OR Ultrasonography OR Ultrasonographic OR Ultrasonic OR Echography AND Sialography OR Sialographies OR “Magnetic resonance imaging” OR “MRI Scan” OR “MR sialography” OR “Computed tomography” OR “SPECT CT” OR “SPECT CT Scan” OR “Multidetector Computed Tomography” OR “Multislice Computed Tomography” OR “Cone-Beam Computed Tomography” OR “Cone-Beam CT Scan” OR “Volume Computed Tomography” OR “Volumetric CT” OR “Volumetric Computed Tomography” OR “Cone-Beam Computer-Assisted Tomography” OR “CAT Scan, Cone-Beam” OR “Cone-Beam Computerized Tomography” OR “Cone-Beam CT” OR “Volume CT” AND “Sialitis” OR “Sialitides” OR Sialadenitis OR Sialoadenitis OR Sialadenitides OR “Sialoadenitides” OR “Sialolith” OR Sialolithiasis OR “Sialolithiasis” OR “Salivary Gland Adenitis” OR “Salivary Gland Adenitides” OR “Salivary Gland Calculi” OR “Salivary Gland Calculus” OR “Salivary Gland Stone” OR “Salivary Gland Inflammation” OR “Salivary calculi” OR “Salivary calculus” OR “Salivary stone” OR “Salivary duct calculi” OR “Salivary duct calculus” OR “Salivary duct stone” OR “Salivary duct inflammation” OR “Parotitis”.

Searches in Google Scholar and in Open Grey, limited to the first 200 hits were also conducted.¹² A manual search in the reference list of the included articles was performed as well. After all, for studies whose full texts were unavailable, contact with authors was made. Duplicate hits were removed from the list upon identification in the software EndNote Web (Clarivate, Philadelphia, PA, USA).

2.3 STUDY SELECTION

The selection of the studies was performed in two phases. In phase 1, two independent reviewers evaluated the title and abstract of each reference retrieved. References whose title and abstract met the eligibility criteria were included straight away. References whose title and abstract did not provide sufficient information for a decision on inclusion/exclusion were assessed in phase 2, when the independent reviewers assessed the full text. References whose full text met the eligibility criteria were included as well. Discrepancies between reviewers regarding inclusion or exclusion of the study were resolved with a new assessment of the reference and discussion between the two reviewers.

2.4 DATA COLLECTION PROCESS

The data of the included articles were extracted by one reviewer independently and a second reviewer cross-checked. The information thoroughly the following data were extracted: last name of the first author and date of publication of the article, country, sample size, information on the condition assessed and the reference test employed, statistical analysis used, and results and discrepancies were resolved with a new assessment of the reference and discussion between the two reviewers of the systematic review and meta-analysis. For missing information on included studies data, the authors were contacted.

2.5 DATA ITEMS

The data extracted from the included studies were: last name of the first author, year of publication of the article, country where the study had been carried out, sample size, information on the condition and the standard test used, information on the statistical analysis employed, and results of the comparison between the ultrasonography and the other imaging methods for the diagnosis of inflammatory and obstructive disorders of the MSG (accuracy, sensibility, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio).

2.6 QUALITY ASSESSMENT

The risk of bias was measured using the revised tool for the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2)³, as shown in the Supplementary file 1. The following four items were evaluated: selection of participants, the assessment of the index test (ultrasonography), the diagnostic test used as a reference, and the time between the assessment of the outcome with the index test (ultrasonography) and the evaluation of the outcome with the reference test. Applicability concerns were also evaluated. The following three items were assessed: patient selection, index test, and reference standard. For each item, each study could be classified as a low risk of bias study or a high risk of bias study.

2.7 SYNTHESIS OF RESULTS

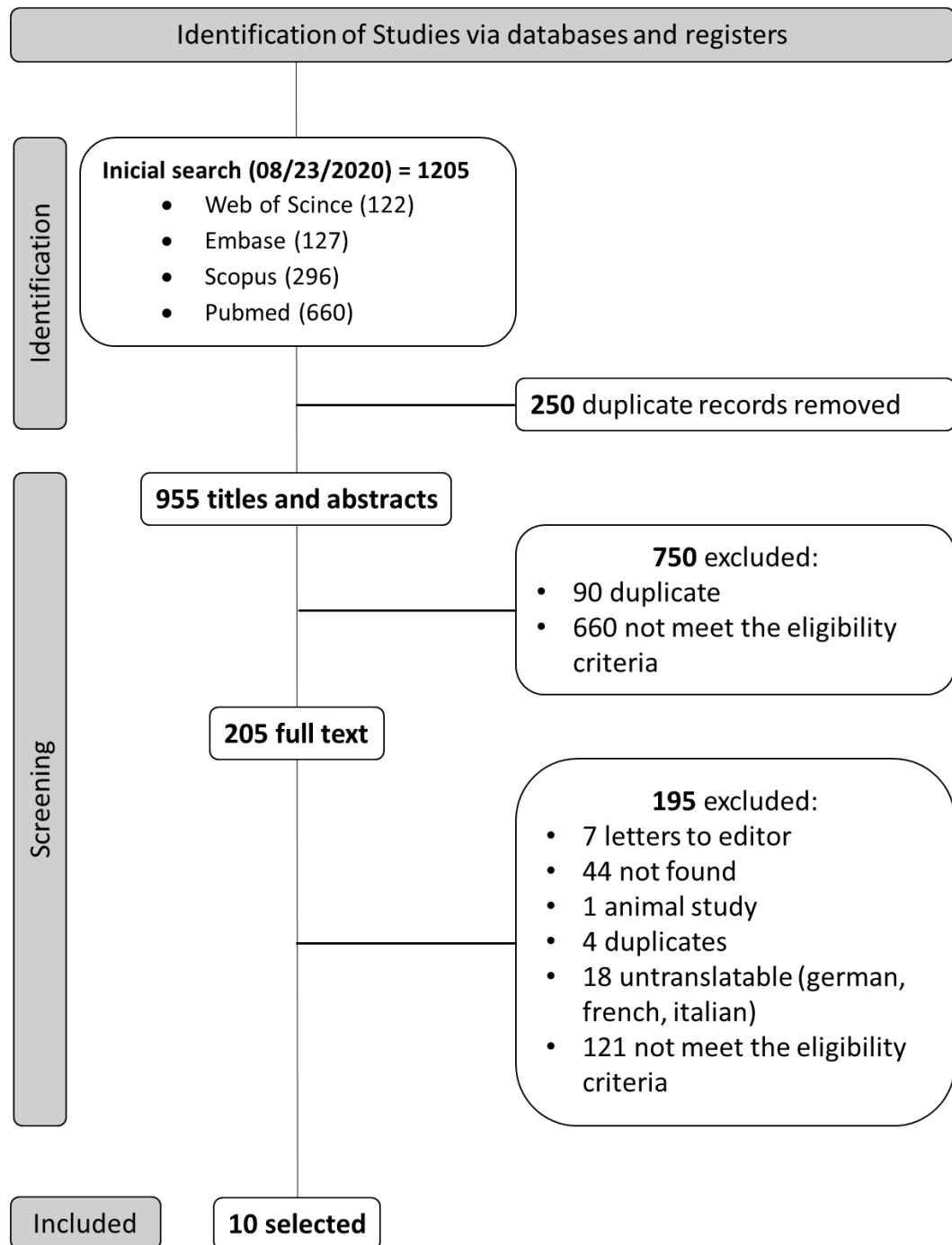
The results of studies with similar methods were aggregated. Meta-analyses were conducted with the MedCalc statistical software, version 19.2.6 (MedCalc Software bv, Ostend, Belgium; <https://www.medcalc.org>; 2020).

3 RESULTS

3.1 STUDY SLECTION PROCESS

The selection process of references included in this systematic review and meta-analysis is presented in the form of a flow chart (Figure 1). A total of 1.205 records were identified in the searches in the four electronic databases. After the removal of 250 duplicates, 955 references remained. The title and abstract of the 955 references were assessed regarding eligibility. A total of 750 studies were excluded and 205 references were selected for full text assessment. The full texts of 44 articles were not found (Appendix). Attempts to purchase the article online were performed, but some studies were unavailable. Among the 205 references whose full texts were evaluated, 10 met the eligibility criteria and were included in systematic review and only four in meta-analysis.

Figure 1. Flowchart of the systematic review and meta-analysis.



3.2 CHARACTERISTICS OF INCLUDED STUDIES

The included articles were 10 diagnostic accuracy studies⁴⁻¹³. Date of publication was between 1989 and 2020, and the language of publication was English. The studies were conduct in Austria⁷, Czech Republic¹⁰, Germany^{5,6,8,11}, Hong Kong⁹, Turkey⁴, Switzerland¹² and United States of America¹³. In five studies sialendoscopy^{5,6,9-11} was used as standard test, sialography in three^{4,7,10}, computed tomography^{9,13} and

magnetic resonance^{8,9} in two. Clinical follow-up⁷, plain radiography⁹, CBCT¹¹, and histopathology⁷ were comparative methods applied only once.

3.3 SAMPLE CHARACTERISTICS

The sample size ranged from 24 to 2,052 individuals. Seven studies had a sample with less than 80 participants.^{4,8-13} In three studies⁵⁻⁷, the number of participants exceeded 600. Two studies evaluated patients between 1-89 years old^{5,7}. In four studies, individuals ranged in age between seven and 7-82 years old took part in the survey^{4,9-12}. Two studies reported only the mean age of the participants^{6,11}. One study reported the mean age of men and women separately only¹³ and another one did not provide information about age or the mean age of the participants⁸. In all included articles male and female individuals were recruited. The characteristics of the included studies are displayed in Supplementary File 2.

4 RESULTS OF THE INDIVIDUAL STUDIES

The pathological condition most commonly analysed was sialolithiasis, found in eight studies.^{2-4,6-10} Only two studies^{1,5} described benign or malignant tumors as the most prevalent pathologies. There have been studies comparing US with sialography^{1,5} sialendoscopy^{4,7,9} or MRI⁸. There were simultaneous comparisons of US with sialography and sialendoscopy^{2,9} with sialendoscopy, and CBCT⁶ as well as with CT and sialendoscopy³. Of the ten studies included in this review and meta-analysis, only four^{8-10,12} presented US accuracy values, being, respectively, 95%, 94.8%, 96% and 85%.

In two articles, the sialoendoscopy was the most accurate method for examination of ductal pathology.^{2,10}

Two studies exhibited the accuracy of MR sialography similar to digital sialography, both superior in relation to US.^{8,9}

The studies confirmed the good diagnostic value of US for several pathologies, such as benign tumors and salivary calculi. The accuracy, sensitivity, specificity, PPV, and NPV ranged between 85-95%, 50-77%, 67,7-100% and 10,5-78%, respectively.

Two studies were focused on the importance of US in the diagnosis of inflammatory diseases.^{1,5} Otherwise, in cases of chronic inflammation, it was unspecific.

One study revealed that CBCT is capable of diagnosing sialoliths in general and tended to be more sensitive than US.⁶

Finally, a retrospective cohort study showed that US and CT complement each other to optimize diagnosis.³

4.1 QUALITY ASSESSMENT

The assessment of risk of bias of the included studies is shown in Supplementary File 1. For patient selection and reference standard, all included studies had low risk of bias. For the selected index test, one study¹³ presented low risk of bias. Considering flow and timing, one study had high risk of bias.⁴

As regards applicability concerns, all included studies had low risk of bias for patient selection and reference standard, but for index test one study¹³ had unclear risk and one presented high risk of bias.⁴

4.2 SYNTHESIS OF THE META-ANALYSES

Only comparisons between US and sialendoscopy for the diagnosis of sialolithiasis were feasible for the present meta-analyses. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were assessed. The standard error was calculated by dividing the subtraction of the upper limit and the lower limit of the confidence interval by 3.92, an established formula stated by the Cochrane Collaboration in its Handbook for Systematic Reviews¹⁴. The results of the meta-analyses demonstrated that sensitivity of the US was 80.0% (confidence interval = 68.7% - 91.3%, I² = 90.54) (Figure 2), specificity was 94.6% (confidence interval = 93.2% - 95.9%, I² = 0.00%) (Figure 3), positive predictive value was 96.2% (confidence interval = 90.8% - 99.9%, I² = 0.00%) (Figure 4), and negative predictive value was 44.7% (confidence interval = 1.00% - 91.5%, I² = 97.82%) (Figure 5).

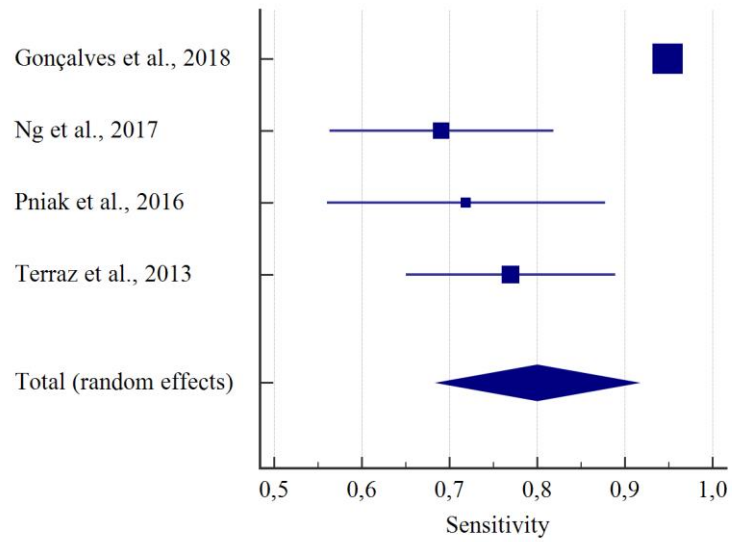
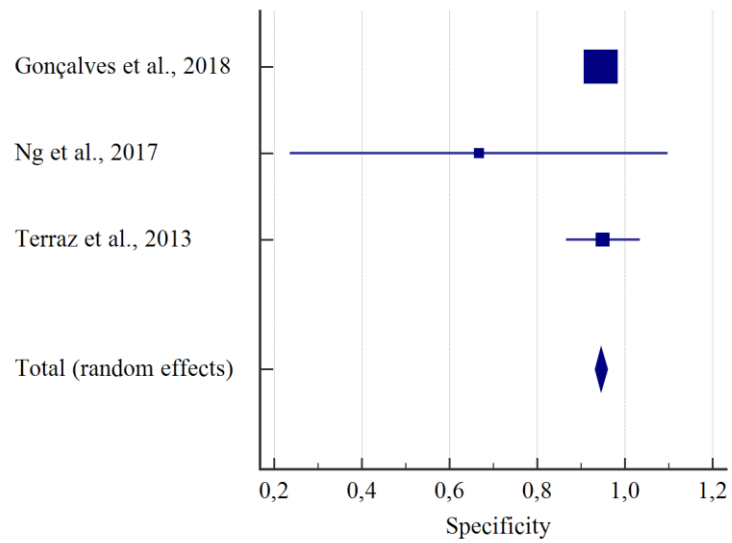
Figure 2. Sensitivity of ultrasound compared to sialendoscopy.**Figure 3.** Specificity of ultrasound compared to sialendoscopy.

Figure 4. Positive predictive value of ultrasound compared to sialendoscopy.

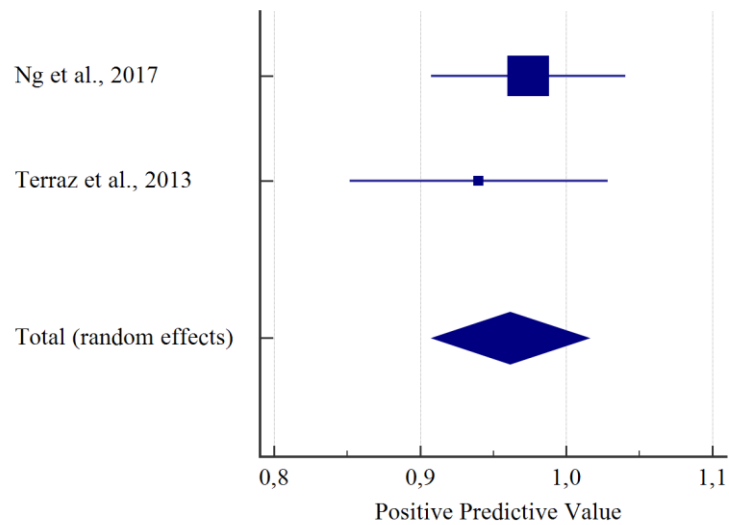
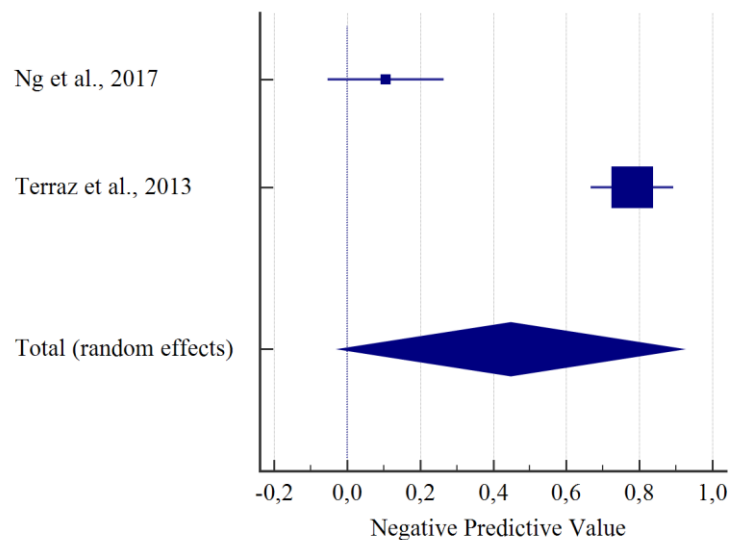


Figure 5. Negative predictive value of ultrasound compared to sialendoscopy.



DISCUSSION

The clinical diagnosis of inflammatory processes of the MSG is difficult, due to the variability of causes and the similarity of their signs and symptoms with several other alterations. Complementary exams commonly used in the oral health care of individuals with complaints involving MSG are often inconclusive, due to the quite non-specific appearance of the images. The identification of an imaging diagnostic method that can contribute more efficiently to the diagnosis of these alterations becomes, therefore, important for the improvement of diagnostic accuracy.

Inflammatory alterations are mainly caused by benign salivary gland obstructions, the most frequently salivary gland disease. The main symptom is painful recurrent swelling and the clinical findings include muddy discharge from the salivary duct. The most widely used imaging diagnostic tools for management of these alterations are sialoendoscopy^{4,9}, ultrasound¹², plain radiography⁹, magnetic resonance⁸, computed tomography or CBCT¹³ and sialography⁹.

The use of US for this diagnostic purpose has several advantages, such as safety and the possibility of evaluating images in real time. US is also more accessible and less expensive than other methods. In fact, there have been no known harmful effects, since the US does not expose patients to ionizing radiation, making the procedure safer than other diagnostic techniques, such as CBCT or plain radiography^{6,12}. Furthermore, this method provides images of soft tissues, which is crucial for this purpose. Otherwise, some of the disadvantages are the need of an experienced operator, considering that it is a scanning method in which the images are displayed instantaneously. Other shortcoming is the possibility of changes on the typical imaging aspect of anatomical references, caused by changes of the probe positioning on the skin. The possibility of storing images in videos can contribute to reducing the dependence of the examiner for the exam.⁶

The diagnostic value of US has been demonstrated, but the comparative assessment of its diagnostic accuracy to other methods used for the diagnosis of inflammatory changes of the MSG needed to be performed. This idea is the central premise of the present systematic review and meta-analysis, whose results may contribute to improve the guidance of clinicians in the evaluation of patients with complaints involving MSG.

After removing studies that did not meet the inclusion criteria, the present systematic review and meta-analysis evaluated 10 articles.⁴⁻¹³ Of these, the first study evaluating US for the diagnosis of salivary gland diseases dates back to 1989⁷. The sample size of the included studies ranged from 24 to 2052. Once US presented good diagnostic value for pathologies in general, some studies recommended US as the exam for the first care of patients with complaints involving MSG, followed by sialendoscopy, in case of need to investigate small calcifications in the ductal system.^{4,5,7}

The quality assessment of the selected studies revealed some shortcomings of the sample. It was included a study that presented high risk of bias¹, related to the flow

and timing. Their US images were obtained after cannulating of the main ducts and contrast injections used in sialographies, which may have compromised the results of the US because of the movement artifacts and the presence of dental prostheses that may have a strong influence on the results. As result, this relevant issue compromised the applicability concern of its index test. Another article, which conducted a retrospective study³, presented unclear risk of bias related to the index test and its applicability concern, due to have not been identified the technique and extent of US examinations included in the sample.

The meta-analysis showed that in order to rule out the diagnosis of inflammatory and obstructive disorders of the MSG, the high sensitivity of US in relation to sialendoscopy, has a high negative predictive value, that is, when a negative result is less likely that the patient has some alteration. On the other hand, when the US method is applied with the intention of diagnosing a certain alteration, it was also possible to observe high specificity, which, consequently, results in a greater impact on the positive predictive value, that is, if the evaluation with US gives a positive result, it is very unlikely that the patient does not actually have alterations in the MSG.

It is also important to mention that although the US accuracy values were high, most studies indicated that the other reference methods were superior for the diagnosis of certain conditions. US was helpful in detecting non-opaque intraductal salivary calculi, but for the evaluation of chronic inflammatory diseases gave non-specific information^{4,8} or only detected advanced cases⁷. Although it was not a goal of the present systematic review and meta-analysis, the description of the typical image of the conditions assessed may also contribute to improve of knowledge about the potentialities of the US for the diagnosis of MSG's inflammatory changes.

Regarding the high diagnostic accuracy of sialendoscopy for sialolithiasis, it is emphasized that its direct visualization inside the ductal system enables it to detect even small calculus located inside the ducts, with the advantage of allowing its immediate removal, in some cases. However, this method presents limitation in the evaluation of glandular parenchyma, which reduces its ability for evaluating other pathologies and inflammatory changes of the MSG. Its efficacy as a therapeutic method was not the objective of the present study and, considering the presented data, it was not possible to reach a conclusion about its risk as an invasive method for diagnoses of inflammatory changes of MSG.

Despite this findings, new researches comparing US with other imaging methods in the assessment of MSG inflammatory and obstructive diseases will help to improve knowledge about its diagnostic accuracy. However, it is important to note that prospective studies comparing US with radiologic examination tools like CBCT may involve unfavorable side effects/risks and may lead to ethical concerns. The occurrence of artifacts and considerations regarding limitations on the evaluation of soft tissues using CBCT must also be discussed^{4,6,7,13}. Considering the application of MRI methods, the presence of dental prostheses, lower cost-effectiveness and the need to inject contrast material are also important issues¹².

The present systematic review and meta-analysis has some limitations. Few studies meeting the eligibility criteria were available and, therefore, the evaluation of well-designed studies comparing US with other diagnostic imaging methods is not so robust. It is important to emphasize this and question in which situations US is indicated and if there is any valid questioning for such results and for future and more enlightening studies.

In conclusion, the high values found for sensitivity and specificity presented by US found by the present systematic review and meta-analysis show that US are suitable as the method of choice for diagnosis in patients with inflammatory and obstructive symptoms involving the MSG. In addition, non-exposure to radiation, real-time visualization of soft tissues, vascular flow evaluation, high availability, and low financial cost for the broad examination justify, in themselves, the indication of US as an important method for evaluating the pathologies studied.

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4 CONSIDERAÇÕES FINAIS

O estudo da acurácia diagnóstica da ultrassonografia na avaliação de doenças inflamatórias e obstrutivas das glândulas salivares maiores tem muito a avançar. Apesar de ser uma técnica adequada para a avaliação destas condições, ainda são poucos os estudos comparativos que apresentam resultados de acurácia, com teste de referência e método de análise padronizado, ou seja, estudos díspares. Ao comparar os estudos que atendem a esses critérios, conclui-se que há diferenças significativas dos resultados da US em relação a, por exemplo, o método da sialoendoscopia. Devido às limitações do estudo, como tamanho da amostra, mais estudos são necessários.

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APÊNDICE - A**DADOS EXTRAÍDOS DOS ARTIGOS SELECIONADOS**

Appendix and Supplementary Files (1, 2 and 3).

[https://drive.google.com/drive/folders/1p41F5aTa8NUZaZqEcGZCP4j_dmbXQFv ?
usp=sharing](https://drive.google.com/drive/folders/1p41F5aTa8NUZaZqEcGZCP4j_dmbXQFv?usp=sharing)