UNIVERSIDADE FEDERAL DE MINAS GERAIS
Faculdade de Odontologia
Colegiado de Pós-Graduação em Odontologia

Bethânia Lara Silveira Freitas

AVALIAÇÃO ULTRASSONOGRÁFICA DE GLÂNDULAS SALIVARES POR ELASTOGRAFIA NA DOENÇA DE SJÖGREN: *DESENVOLVIMENTO DE UM PROTOCOLO PARA O EXAME E REVISÃO SISTEMÁTICA COM METANÁLISE*

Belo Horizonte
2025

Bethânia Lara Silveira Freitas

AVALIAÇÃO ULTRASSONOGRÁFICA DE GLÂNDULAS SALIVARES POR ELASTOGRAFIA NA DOENÇA DE SJÖGREN: *DESENVOLVIMENTO DE UM PROTOCOLO PARA O EXAME E REVISÃO SISTEMÁTICA COM METANÁLISE*

Dissertação apresentada ao Colegiado de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Minas Gerais, como requisito parcial à obtenção do grau de Mestre em Odontologia - área de concentração em Estomatologia

Orientadora: Profa. Dra. Sílvia Ferreira de Sousa
Coorientadora: Profa. Dra. Tarcília Aparecida da Silva

Belo Horizonte
2025

Ficha Catalográfica

F866a
2025
T

Freitas, Bethânia Lara Silveira.
Avaliação ultrassonográfica de glândulas salivares por elastografia na doença de Sjögren: desenvolvimento de um protocolo para o exame e revisão sistemática com metanálise / Bethânia Lara Silveira Freitas. -- 2025.

75 f. : il.

Orientadora: Sílvia Ferreira de Sousa.
Coorientadora: Tarcília Aparecida da Silva.

Dissertação (Mestrado) -- Universidade Federal de Minas Gerais, Faculdade de Odontologia.

1. Doenças autoimunes. 2. Técnicas de imagem por elasticidade. 3. Glândulas salivares. 4. Síndrome de Sjögren. 5. Ultrassonografia. I. Sousa, Sílvia Ferreira de. II. Silva, Tarcília Aparecida da. III. Universidade Federal de Minas Gerais. Faculdade de Odontologia. IV. Título.

BLACK - D047

Elaborada por: Miriam Cândida de Jesus - CRB 6/2727.

UNIVERSIDADE FEDERAL DE MINAS GERAIS

FACULDADE DE ODONTOLOGIA

COLEGIADO DO CURSO DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

FOLHA DE APROVAÇÃO

AVALIAÇÃO ULTRASSONOGRÁFICA DE GLÂNDULAS SALIVARES POR ELASTOGRAFIA NA DOENÇA DE SJÖGREN: DESENVOLVIMENTO DE UM PROTOCOLO PARA O EXAME E REVISÃO SISTEMÁTICA COM METANÁLISE

BETHÂNIA LARA SILVEIRA FREITAS

Dissertação submetida à Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação em ODONTOLOGIA, como requisito para obtenção do grau de Mestre em ODONTOLOGIA, área de concentração ESTOMATOLOGIA.

Aprovada em 14 de julho de 2025, pela banca constituída pelos membros:

Profa. Sílvia Ferreira de Sousa - Orientadora
Faculdade de Odontologia da UFMG

Profa. Tarcília Aparecida da Silva
Faculdade de Odontologia da UFMG

Profa. Jeane de Fátima Correia Silva Alves
Centro Universitário Newton Paiva

Profa. Maria Cássia Ferreira de Aguiar
Faculdade de Odontologia da UFMG

Belo Horizonte, 14 de julho de 2025.

Documento assinado eletronicamente por **Silvia Ferreira de Sousa**, **Professora do Magistério Superior**, em 14/07/2025, às 16:28, conforme horário oficial de Brasília, com fundamento no art. 5º do Decreto nº 10.543, de 13 de novembro de 2020.

Documento assinado eletronicamente por **Tarcilia Aparecida da Silva**, **Professora do Magistério Superior**, em 14/07/2025, às 16:29, conforme horário oficial de Brasília, com fundamento no art. 5º do Decreto nº 10.543, de 13 de novembro de 2020.

Documento assinado eletronicamente por **Maria Cassia Ferreira de Aguiar**, **Professora do Magistério Superior**, em 14/07/2025, às 16:30, conforme horário oficial de Brasília, com fundamento no art. 5º do Decreto nº 10.543, de 13 de novembro de 2020.

Documento assinado eletronicamente por **Jeane de Fátima Correia Silva Alves**, **Usuário Externo**, em 14/07/2025, às 16:31, conforme horário oficial de Brasília, com fundamento no art. 5º do Decreto nº 10.543, de 13 de novembro de 2020.

A autenticidade deste documento pode ser conferida no site https://sei.ufmg.br/sei/controlador_externo.php?acao=documento_conferir&id_orgao_acesso_externo=0, informando o código verificador **4318612** e o código CRC **3D3EC237**.

Dedico este trabalho às pessoas de bem que iluminam meu caminho.

AGRADECIMENTOS

Agradeço a Deus, maior fonte de amor e bondade, por me fortalecer em cada desafio e por renovar a minha fé, lembrando-me que a vida sempre reserva o melhor para nós.

Aos meus pais Luiz Geraldo e Cornélia e irmãos Guilherme e Henrique, agradeço por me ensinarem valores essenciais da vida: amor, bondade e respeito. À minha madrinha Marísia, pelo cuidado e atenção dedicados. Aos meus avós (in memoriam) por serem a fortaleza de toda a família e a todos os meus familiares que caminham ao meu lado. Nada seria possível sem o apoio e a presença de cada um de vocês, obrigada!

Aos meus amigos, agradeço a presença constante em minha vida, tornando a caminhada mais leve, prazerosa e repleta de significado. Não há riqueza maior do que compartilhar a vida com pessoas do bem!

Aos colegas de profissão, auxiliares, recepcionistas e funcionários do Setor de Odontologia do SEST, agradeço todo carinho e parceria. Um agradecimento especial à Paula Duque, cuja dedicação foi fundamental para que eu conciliasse o mestrado com minhas atividades profissionais. Obrigada!

À equipe da Estomatologia/Patologia da FAO-UFMG, pelo conhecimento compartilhado e por transformar esses dois anos em um período de aprendizado e crescimento imensurável. Um agradecimento especial à Profa. Sílvia, minha orientadora, pelo apoio e ao Prof. Maurício, colaborador essencial deste projeto, companheiro e amigo, cujo cuidado com o próximo e amor à profissão foram inspiradores. Agradeço a Profa. Tarcília, Alcides, Laiz, Fernanda, Clara, Mariana e toda equipe, pelo trabalho que gera um impacto positivo na vida dos pacientes.

Aos técnicos do laboratório de patologia e funcionários da FAO-UFMG, pela dedicação diária que sustenta este projeto. À Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), à Organização Rotary e à Universidade Federal de Minas Gerais (Fundo Fundep), pelo apoio financeiro.

Finalizo com um agradecimento especial a todos os pacientes que confiaram a mim e a esta equipe suas histórias, dificuldades e esperanças. Foi um privilégio pertencer a este projeto e contribuir de alguma forma. Muito obrigada, de coração!

“Vivendo se aprende; mas o que se aprende, mais, é só a fazer outras maiores perguntas.”

Guimarães Rosa

RESUMO

A Doença de Sjögren (DS) é uma desordem autoimune caracterizada por infiltração linfocítica das glândulas salivares, o que pode levar ao aumento da fibrose glandular. A elastografia por onda de cisalhamento (SWE, do inglês *shear wave elastography*) é uma técnica de ultrassonografia que quantifica a rigidez tecidual pela mensuração da velocidade de propagação da onda, expressa em velocidade em metros por segundo (m/s) ou como módulo de elasticidade em kilopascal (kPa). Publicações têm demonstrado que a SWE possa contribuir no diagnóstico entre pacientes com DS e controles. Entretanto, a literatura atual também carece de padronização na execução da SWE para avaliar as glândulas salivares na DS. Este trabalho teve como objetivos (i) desenvolver um protocolo padronizado para a aplicação da SWE nas glândulas salivares maiores da DS; (ii) e avaliar sistematicamente seu desempenho diagnóstico conforme os critérios de classificação do Colégio Americano e Liga Europeia de Reumatologia (ACR/EULAR) 2016. A metodologia combinou um estudo-piloto prospectivo com nove participantes do sexo feminino pareadas por idade (três com DS, três com sintomas secos sem DS e três controles saudáveis) avaliadas por SWE bilateralmente, nos planos longitudinal e transversal das parótidas e submandibulares, em três regiões diferentes de cada glândula; e uma revisão sistemática com meta-análise envolvendo 11 artigos e 1.029 pacientes. Os resultados da série de casos demonstraram variação nas medidas de SWE entre diferentes planos e regiões glandulares nos três grupos de indivíduos. Os resultados da meta-análise mostraram valores de SWE significativamente maiores em pacientes com DS, com a elastografia da glândula parótida apresentando maior acurácia diagnóstica em comparação à submandibular (82,9% vs. 73,1%). Nenhum dos estudos classificou as alterações ultrassonográficas pelo consenso OMERACT, limitando a comparabilidade dos dados obtidos na SWE com a classificação OMERACT. Observou-se ainda, heterogeneidade metodológica nos estudos existentes, principalmente quanto à realização do exame . Nosso estudo concluiu que há uma necessidade da padronização de protocolos da SWE para melhorar sua acurácia diagnóstica e promover sua integração clínica. A metanálise reforça a eficácia da técnica na diferenciação entre pacientes com DS e controles saudáveis, particularmente na avaliação da glândula parótida. Este trabalho apresenta recomendações para padronização de uma técnica reprodutível, não-invasiva para DS, incluindo a necessidade de consenso sobre parâmetros técnicos.

Palavras-chave: doenças autoimunes; elastografia; glândulas salivares; doença de Sjögren; ultrassonografia.

ABSTRACT

Ultrasonographic evaluation of salivary glands by elastography in Sjögren's Disease: development of an examination protocol and systematic review with meta-analysis

Sjögren's Disease (SD) is an autoimmune disorder characterized by lymphocytic infiltration of the salivary glands, which may lead to increased glandular fibrosis. Shear wave elastography (SWE) is an ultrasound technique that quantifies tissue stiffness by measuring the propagation speed of shear waves, expressed either in meters per second (m/s) or as elasticity modulus in kilopascals (kPa). Recent publications have shown that SWE may aid in distinguishing patients with SD from healthy controls. However, current literature lacks standardized protocols for performing SWE to assess salivary glands in SD. This study aimed to (i) develop a standardized protocol for the application of SWE to the major salivary glands in SD, and (ii) systematically evaluate its diagnostic performance according to the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria. The methodology combined a prospective pilot study with nine age-matched female participants (three with SD, three with sicca symptoms without SD, and three healthy controls) who underwent bilateral SWE of the parotid and submandibular glands in both longitudinal and transverse planes, with three regions evaluated in each gland; and a systematic review with meta-analysis involving 11 articles and 1,029 patients. The case series revealed variations in SWE measurements across different planes and glandular regions in all three groups. The meta-analysis showed significantly higher SWE values in SD patients, with parotid gland elastography demonstrating higher diagnostic accuracy compared to submandibular gland elastography (82.9% vs. 73.1%). None of the studies classified ultrasonographic changes using the OMERACT consensus, limiting the comparability of SWE data with OMERACT classification. Additionally, methodological heterogeneity was observed in existing studies, particularly regarding examination procedures. Our study concluded that standardization of SWE protocols is necessary to improve diagnostic accuracy and facilitate clinical integration. The meta-analysis supports SWE's efficacy in differentiating SD patients from healthy controls, particularly in parotid gland assessment. This work provides recommendations for standardizing a reproducible, non-invasive technique for SD, including the need for consensus on technical parameters.

Keywords: autoimmune diseases; elastography; salivary glands; Sjögren Disease; ultrasonography.

LISTA DE ABREVIATURAS E SIGLAS

2D-SWE	2D shear wave elastography
ACR	American College of Rheumatology
AECG	American European Consensus Group
ARFI	Acoustic Radiation Force Impulse
DS	Doença de Sjögren
EULAR	European League Against Rheumatism
FAN	Fator Antinuclear
Kpa	Kilopascal
m/s	Metros por Segundo
OMERACT	Outcome Measures in Rheumatology
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ROI	Regions of Interest
SE	Strain Elastography
SWE	Shear Wave Elastography
UGS	Ultrassonografia das Glândulas Salivares
US	Ultrassonografia

SUMÁRIO

1 CONSIDERAÇÕES INICIAIS 10
2 OBJETIVOS 14
2.1 Objetivo Geral 14
2.2 Objetivos específicos 14
3 METODOLOGIA EXPANDIDA 15
3.1 Protocolo e registro da revisão sistemática 15
3.2 Delineamento do estudo 15
3.2.1 Processo de triagem 15
3.2.2 Extração dos dados 16
3.2.3 Avaliação do risco de viés do estudo 16
3.3 Estabelecimento e aprovação ética 16
3.4 Participantes e critérios de elegibilidade 17
3.5 Avaliação por elastografia por onda de cisalhamento 17
3.6 Análise dos dados 18
4 RESULTADOS E DISCUSSÃO 19
4.1 Os resultados e discussão serão apresentados no formato do Artigo intitulado "*Shear wave elastography of salivary glands in Sjögren disease: a novel protocol and systematic review with meta-analysis*" submetido ao periódico Dentomaxillofacial Radiology (fator de impacto: 2.9; Online ISSN 1476-542X; extrato QUALIS A2) 19
5 CONSIDERAÇÕES FINAIS 66
REFERÊNCIAS 67
APÊNDICE A – Aprovação do Comitê de Ética em Pesquisa 74

1 CONSIDERAÇÕES INICIAIS

A Doença de Sjögren (DS) é uma doença autoimune multissistêmica, caracterizada por infiltração linfocítica crônica dos tecidos lacrimais e salivares, resultando na destruição progressiva dessas glândulas exócrinas (Zhan *et al.*, 2023; Chen *et al.*, 2016). A apresentação clínica típica inclui xerostomia (boca seca), xeroftalmia (secura ocular), fadiga e poliartralgia (Arslan *et al.*, 2020). A xerostomia pode vir acompanhada de hipossalivação, levando à alteração do paladar, dificuldades da mastigação, aumento do desenvolvimento de cáries dentárias e candidíase oral (Psianou *et al.*, 2018), que podem comprometer significativamente a qualidade de vida dos pacientes (Dias *et al.*, 2021).

A transição da nomenclatura de "Síndrome de Sjögren" para "Doença de Sjögren" tem ganhado forças nas diretrizes internacionais, especialmente no recente consenso do Reino Unido, que reconhece a condição como uma entidade clínica distinta com envolvimento de múltiplos órgãos (Baer e Hammitt, 2021; Price *et al.*, 2025). Apesar de uma prevalência global estimada entre 0,005% e 0,01%, a DS continua subdiagnosticada, especialmente em estágios iniciais ou em pacientes soronegativos para Anti-SSA/RO. (Beydon *et al.*, 2024).

O diagnóstico para a DS baseia-se em critérios de classificação que vêm sendo revisados desde 2002, quando o Grupo de Consenso Americano-Europeu (AECG, do inglês *American European Consensus Group*), propôs um conjunto de parâmetros que incluía sintomas orais e oculares, exames histológicos e laboratoriais, sialometria não estimulada, além da biópsia de glândula salivar menor (Vitali *et al.*, 2002). Em 2012, o Colégio Americano de Reumatologia (ACR, do inglês *American College of Rheumatology*) propôs uma outra versão com critérios baseados exclusivamente em testes objetivos, que praticamente não contemplavam o envolvimento morfológico e funcional das glândulas salivares maiores (Shiboski *et al.*, 2012; Cindil *et al.*, 2018). Em 2016, o Colégio Americano de Reumatologia/Liga Europeia contra o Reumatismo (ACR/EULAR, do inglês *American College of Rheumatology/European League Against Rheumatism)* propuseram um novo conjunto de critérios de classificação para a DS, baseados em cinco testes objetivos com pesos distintos: 3 pontos para biópsia de glândula salivar menor com focus score ≥ 1; 3 pontos para positividade do autoanticorpo Anti-SSA/Ro; 1 ponto para teste de

coloração ocular ou Van Bijsterveld; 1 ponto para teste de Schirmer; e 1 ponto para taxa de fluxo salivar não estimulado ≤ 0,1mL/min. O diagnóstico é estabelecido nos casos em que a pontuação é igual ou superior a 4. Nestes novos critérios, o comprometimento das glândulas salivares é documentado através da biópsia de glândula salivar menor e/ou pela sialometria não estimulada (Shiboski *et al.*, 2017). O diagnóstico da DS se baseia, portanto, em parâmetros clínicos, sorológicos e microscópicos, sendo a biópsia das glândulas salivares o padrão ouro para diagnóstico (Fisher *et al.*, 2017). A biópsia é um procedimento realizado para avaliar o grau de infiltração linfocítica nas glândulas salivares menores, uma característica da DS. Por se tratar de um procedimento invasivo, pode ocasionar desconforto ao paciente e complicações como dor, edema ou infecção, parestesia labial, embora sejam leves e de resolução espontânea (AlMannai *et al.*, 2024).

Indivíduos que apresentam sintomas de olho seco e/ou boca seca (xerostomia e/ou hipossalivação), mas que não atendem aos critérios estabelecidos pelo ACR/EULAR para DS, são categorizados como portadores de síndrome sicca sem DS (Oliveira et al., 2022). Essa distinção é relevante para a investigação diagnóstica, uma vez que esses pacientes apresentam manifestações clínicas semelhantes, mas não preenchem os critérios formais da doença.

A ultrassonografia das glândulas salivares (UGS) emergiu como um método de imagem não invasivo com potencial de aplicação ao diagnóstico e manejo da DS. A avaliação por UGS baseia-se na homogeneidade do parênquima e na ecogenicidade das glândulas salivares, analisando os danos estruturais (Fana e Terslev, 2024). Com o objetivo de simplificar o uso do ultrassom no diagnóstico de pacientes com DS, o grupo de trabalho em ultrassonografia da *Outcome Measures in Rheumatology* (OMERACT) desenvolveu e validou em 2019 um sistema de pontuação semiquantitativa de quatro graus de gravidade para as glândulas parótidas e submandibulares, visando eliminar a diversidade de sistemas de pontuação utilizados e, contribuir assim, para estimular a UGS como método auxiliar no diagnóstico e manejo da DS. Esse sistema classifica os achados ultrassonográficos em: grau 0 - parênquima normal; grau 1 - alteração mínima, caracterizada pela heterogeneidade leve sem áreas anecóicas ou hipoecóicas; grau 2 - alteração moderada, com heterogeneidade moderada e presença de áreas focais anecóicas ou hipoecóicas; e grau 3 - alteração grave, evidenciada por heterogeneidade difusa e áreas anecóicas ou hipoecóicas ocupando toda a superfície glandular (Jousse-Joulin *et al.*, 2019).

Estudos recentes demonstraram que a incorporação desse sistema de pontuação OMERACT aos critérios classificatórios da ACR/EULAR 2016 resultou em um bom desempenho diagnóstico, com impacto semelhante ao dos itens de menor peso nos referidos critérios (Jousse-Joulin *et al.*, 2020; Robin *et al.*, 2022).

No entanto, apesar de resultados promissores demonstrando inclusive que a UGS pelo sistema OMERACT poderia em alguns casos suprimir a realização da biópsia (Fana *et al.*, 2021), a UGS permanece excluída dos critérios de classificação mais recentes da ACR/EULAR, (van Nimwegen *et al.*, 2020; Shiboski *et al.*, 2017), permanecendo como instrumento auxiliar e não como medida de desfecho (Tabaa *et al.*, 2021; Jousse-Joulin *et al.*, 2020). É possível que a heterogeneidade de sistemas de pontuação, a dependência do operador e a variabilidade na interpretação das imagens dificultem a integração da ultrassonografia nos algoritmos diagnósticos (Martins *et al.*, 2024).

Alterações morfológicas microscópicas podem ser detectadas ao longo do curso da DS, sendo a fibrose do parênquima salivar (Karadeniz *et al.*, 2023), decorrente da atividade inflamatória, uma delas. De acordo com Zhang *et al.* (2016), pacientes com DS podem apresentar um aumento na rigidez glandular, reflexo de alterações estruturais do parênquima. No exame de UGS com o sistema OMERACT não é possível analisar quantitativamente a fibrose presente (Jousse-Joulin *et al.*, 2019. Por outro lado, a elastografia é uma técnica que permite a análise da rigidez tecidual (Prata *et al.*, 2022). Essa técnica foi inicialmente utilizada na medicina para avaliar a fibrose hepática (Barr, 2018). Nas mamas, tireoide e próstata, a elastografia é utilizada para avaliar a rigidez do tecido, auxiliando na diferenciação entre massas benignas e malignas (Turnaoglu *et al.*, 2018).

Existem três principais métodos de elastografia disponíveis: elastografia por onda de cisalhamento (SWE, do inglês *shear wave elastography*), elastografia baseada em deformação (SE, do inglês *strain elastography*) e a quantificação de imagem por impulso de força de radiação acústica (ARFI, do inglês *acoustic radiation force impulse*) (Lorenzon *et al.*, 2022). A SWE é a técnica mais recente e possibilita a obtenção de informações tanto quantitativas quanto qualitativas sobre a rigidez tecidual, expressas em um parâmetro de velocidade em metros por segundo (m/s) ou como módulo de elasticidade em kilopascal (kPa) (Arslan *et al.*, 2020; Badarinza *et al.*, 2020). Essa técnica oferece maior precisão diagnóstica, uma vez que permite ao operador selecionar e ajustar a região de interesse (ROI, do inglês *regions of interest*)

no tecido alvo, além de dispensar a necessidade de compressão externa (Arslan *et al.*, 2020). Uma variação ainda mais recente é a elastografia por onda de cisalhamento bidimensional (2D-SWE, do inglês 2D shear wave elastography), que possibilita a visualização em tempo real de um elastograma colorido sobreposto à imagem em escala de cinza, fornecendo simultaneamente informações anatômicas e da rigidez tecidual (Ozer *et al.*, 2023). A SE se baseia na aplicação de compressão manual para gerar uma medida qualitativa da elasticidade, porém não oferece dados quantitativos (Cosgrove *et al.*, 2013). Já a ARFI avalia a distribuição de deslocamento provocada por uma força acústica aplicada a diferentes pontos e produz um mapa qualitativo em escala de cinza que reflete variações na rigidez tecidual e na velocidade da onda de cisalhamento (Devauchelle-Pensec *et al.*, 2021; Lorenzon *et al.*, 2022).

Nos últimos anos, vários trabalhos foram publicados utilizando a elastografia como uma ferramenta diagnóstica na DS (Arslan *et al.*, 2020; Karadeniz *et al.*, 2023; Özer *et al.*, 2023; Satış *et al.*, 2020) e têm demonstrado que o aumento da rigidez das glândulas salivares se correlaciona com a gravidade da doença, reforçando a utilidade clínica da elastografia nesse contexto (Liu *et al.*, 2024). No entanto, ainda não há consenso sobre os valores de corte ideais, as técnicas de aquisição ou protocolos padronizados. Além disso, muitos estudos publicados não adotam exclusivamente os critérios de classificação ACR/EULAR de 2016 (van Nimwegen *et al.*, 2020; Shiboski *et al.*, 2017), limitando sua aplicabilidade clínica. A literatura atual também carece de padronização na execução da SWE para avaliar as principais glândulas salivares em pacientes com DS, apresentando grande heterogeneidade em técnicas, parâmetros de medição e protocolos entre os estudos (Karadeniz *et al.*, 2023).

O presente estudo teve, portanto, dois objetivos: propor um protocolo padronizado e reprodutível para a aplicação da SWE na triagem da DS; revisar sistematicamente a literatura e realizar uma meta-análise sobre o desempenho diagnóstico da SWE aplicada às principais glândulas salivares na DS, com base em estudos alinhados aos critérios de classificação ACR/EULAR de 2016.

2 OBJETIVOS

2.1 Objetivo Geral

Propor um protocolo padronizado para a aplicação da SWE na triagem da DS, revisar sistematicamente a literatura e realizar uma metanálise sobre o desempenho diagnóstico da técnica aplicada às glândulas salivares maiores, considerando apenas estudos alinhados aos critérios de classificação ACR/EULAR de 2016.

2.2 Objetivos específicos

- Comparar os valores da elastografia (m/s e Kpa) das parótidas e submandibulares nos planos de análise longitudinal e transversal, considerando registros em 3 regiões anatômicas das glândulas, em indivíduos com DS, com sintomas sicca sem DS e controles saudáveis.

- Extrair dos artigos incluídos na revisão características clínicas demográficas dos grupos DS e controle.

- Extrair dos artigos incluídos na revisão características dos exames de elastografia realizados nos grupos DS e controle.

- Extrair dos artigos incluídos na revisão valores de SWE dos grupos DS e controle.

- Realizar nos artigos incluídos uma metanálise dos valores de SWE dos grupos DS e controle.

- Realizar nos artigos incluídos uma metanálise da performance diagnóstica da SWE na DS.

3 METODOLOGIA EXPANDIDA

Capítulo 1: Revisão sistemática da literatura

3.1 Protocolo e registro da revisão sistemática

Esta revisão sistemática aderiu às diretrizes descritas no *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) (PAGE *et al.*, 2021). Um protocolo foi registrado *no International Prospective Register of Systematic Reviews* (PROSPERO; CRD42024546909).

3.2 Delineamento do estudo

Buscas eletrônicas foram realizadas nas seguintes bases de dados desde sua criação até janeiro de 2025: PubMed, Web of Science, Scopus, Embase, Ovid e LILACS. Nenhuma restrição foi aplicada quanto ao idioma, à data de publicação ou à região geográfica. Buscas manuais nas listas de referências dos artigos incluídos e buscas na literatura cinzenta por meio do Google Scholar (limitadas aos primeiros 200 registros) foram realizadas (Haddaway *et al.*, 2015). Registros duplicados entre as bases foram identificados e removidos usando a plataforma Rayyan (Ouzzani *et al.*, 2016).

3.2.1 Processo de triagem

As referências obtidas por meio das buscas eletrônicas foram triadas de acordo com os critérios de elegibilidade predefinidos. Três autores independentes (B.L.S.F., L.S.J. e A.C.C.P.) conduziram a triagem em duas fases distintas. Na primeira fase, títulos e resumos foram avaliados, e aqueles que pareciam atender aos critérios de elegibilidade foram submetidos a uma avaliação adicional na fase seguinte. Quando os títulos e resumos não forneciam informações suficientes, o texto completo foi analisado. Na segunda fase, os estudos cujo texto completo atendia aos critérios de elegibilidade foram incluídos. Para os estudos sem texto completo disponível, foram feitas tentativas de obtê-los entrando em contato com os autores correspondentes por e-mail. Quaisquer divergências entre os três autores em relação

à seleção dos estudos foram resolvidas mediante discussão e consenso com a participação de um autor sênior (S.F.S.).

3.2.2 Extração dos dados

Os seguintes dados foram extraídos de cada estudo incluído: nome(s) do(s) autor(es) e ano de publicação, país do estudo, tamanho da amostra, características demográficas dos participantes (idade e sexo), glândula salivar analisada, plano de análise e valores de elastografia relatados em m/s e/ou kPa. Também foram registrados dados clínicos dos participantes com DS, contendo duração da doença, atividade da doença, *focus score*, xerostomia, fluxo salivar, xeroftalmia e resultados do teste de Schirmer. Adicionalmente, foram colhidas informações sobre parâmetros sorológicos anti-SSA/Ro, anti-SSB/La, fator reumatoide e anticorpos antinucleares/fator antinuclear (FAN).

3.2.3 Avaliação do risco de viés do estudo

A qualidade metodológica dos estudos incluídos foi avaliada por meio do *Critical Appraisal Checklist do Joanna Briggs Institute* da Universidade de Adelaide, Austrália. Foram empregados critérios para estudos de acurácia diagnóstica (Campbell *et al.*, 2020) e estudos transversais (Moola *et al.*, 2020). Cada item das ferramentas de avaliação foi classificado como "sim" (se o estudo preencheu o critério avaliado), "não" (se o estudo não preencheu o critério avaliado), "pouco claro" (se o estudo não forneceu informações suficientes sobre se o estudo preencheu ou não os critérios) ou "não aplicável". Quaisquer discordâncias entre os autores foram resolvidas por consenso.

Capítulo 2: Proposição metodológica para a padronização do exame

3.3 Estabelecimento e aprovação ética

Este estudo metodológico piloto foi conduzido com uma amostra de conveniência de pacientes atendidos na Faculdade de Odontologia da Universidade

Federal de Minas Gerais, em Belo Horizonte, Brasil. Todos os procedimentos foram realizados em dezembro de 2024. A aprovação ética foi obtida junto ao Comitê de Ética em Pesquisa da instituição (Nº 60804622.9.0000.5149). O estudo seguiu os princípios da Declaração de Helsinque, e todos os participantes forneceram consentimento informado por escrito.

3.4 Participantes e critérios de elegibilidade

Um total de nove mulheres adultas (idade média: 47 anos; faixa etária: 43–49 anos) foram pareadas por idade e distribuídas igualmente em três grupos: DS, sicca sem DS e controles saudáveis. As pacientes com DS foram classificadas de acordo com os critérios de classificação mais recentes da ACR/EULAR (Shiboski *et al*., 2017). Indivíduos com olho seco e/ou boca seca (xerostomia e/ou hipossalivação) que não atendiam aos critérios da ACR/EULAR foram categorizados como sicca sem DS (Oliveira *et al*., 2022). O grupo controle saudável consistiu em indivíduos sem alterações sistêmicas, que estavam recebendo atendimento odontológico na universidade.

Os critérios de exclusão incluíram a presença de outras doenças reumáticas inflamatórias concomitantes, condições coexistentes (por exemplo, HIV, hepatites B ou C, amiloidose, doença do enxerto contra hospedeiro), certos hábitos (por exemplo, tabagismo e/ou consumo de álcool), radioterapia prévia, gravidez, histórico de sialolitíase, estenose do ducto parotídeo ou tumores linfomatosos das glândulas salivares maiores.

3.5 Avaliação por elastografia por onda de cisalhamento

A avaliação ultrassonográfica das glândulas parótida e submandibular foi realizada utilizando um transdutor linear de alta frequência (5–18 MHz) em um sistema de ultrassom LOGIQ P8 (GE Healthcare™, NY, EUA). Todos os procedimentos foram conduzidos por uma cirurgiã-dentista (B.L.S.F.) previamente calibrada em técnicas ultrassonográficas. As medições elastográficas foram posteriormente analisadas por um radiologista oral e maxilofacial (M.A.A.C.), que não tinha conhecimento da alocação dos participantes nos grupos do estudo.

Os exames foram realizados com os pacientes em posição supina, aplicando-se pressão mínima com o transdutor enquanto o paciente prendia a respiração por alguns segundos para reduzir artefatos de movimento. A elastografia foi realizada bilateralmente com medições obtidas em seis ROI's por glândula, sendo três em um plano longitudinal e três em um plano transversal. Cada valor de ROI correspondeu à mediana de 10 medições adquiridas automaticamente pelo sistema em cada região. Os valores da elastografia foram registrados tanto em kPa quanto em m/s.

Para a avaliação da glândula submandibular no plano longitudinal, o transdutor foi posicionado paralelo ao corpo da mandíbula. Inicialmente, a imagem em modo B foi utilizada para delinear a extensão anteroposterior do parênquima glandular, e três pontos de referência foram marcados na pele para garantir o posicionamento padronizado do transdutor: anterior, posterior e intermediária entre as bordas anterior e posterior da glândula. Mantendo o transdutor na posição longitudinal, três regiões foram avaliadas em cada glândula: na glândula submandibular, porção medial (próxima ao vértice do trígono submandibular), intermediária e lateral (adjacente à fossa submandibular). Para as avaliações no plano transversal, os pontos de referência estabelecidos durante a varredura longitudinal foram utilizados para guiar o posicionamento do transdutor. A glândula submandibular foi então avaliada em suas regiões anterior, intermediária e posterior.

Seguindo os mesmos critérios, a glândula parótida foi avaliada em suas regiões anterior, intermediária e posterior no plano longitudinal, e em suas regiões superior, intermediária e inferior no plano transversal. Para aumentar a precisão das medições, todas as avaliações elastográficas foram realizadas com pressão leve e consistente do transdutor, e os pacientes foram instruídos a permanecer imóveis durante o procedimento.

3.6 Análise dos dados

Os dados foram tabulados no Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, EUA) e analisados descritivamente no GraphPad Prism, versão 8.0.0 para Windows (GraphPad Software, San Diego, CA, EUA).

4 RESULTADOS E DISCUSSÃO

4.1 Os resultados e discussão serão apresentados no formato do Artigo intitulado "*Shear wave elastography of salivary glands in Sjögren disease: a novel protocol and systematic review with meta-analysis"* submetido ao periódico **Dentomaxillofacial Radiology** (fator de impacto: 2.9; Online ISSN 1476-542X; extrato QUALIS A2).

ARTIGO

Shear wave elastography of salivary glands in Sjögren disease: a novel protocol and systematic review with meta-analysis

Bethânia Lara Silveira **Freitas**[1*], Laura Silva **Jerônimo**[1*], Ana Clara Coutinho **Pires**[1], Leandro Augusto **Tanure**[2], Débora Cerqueira **Calderaro**[2], José Alcides Almeida de **Arruda**[1,3], Lucas Guimarães **Abreu**[4], Tarcília Aparecida **Silva**[1,5], Maurício Augusto Aquino de **Castro**[1], Sílvia Ferreira de **Sousa**[1]

[1]Department of Oral Surgery, Pathology, and Clinical Dentistry, School of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.
[2]Department of Locomotor System, School of Medicine, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.
[3]Department of Oral Diagnosis and Pathology, School of Dentistry, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.
[4]Department of Child and Adolescent Oral Health, School of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.
[5]Multiprofessional Integrated Residency in Health, Hospital das Clínicas, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

Corresponding author: Prof. Sílvia Ferreira de Sousa. Laboratory of Experimental Pathology II, Department of Oral Surgery, Pathology, and Clinical Dentistry, School of Dentistry, room 3203, Universidade Federal de Minas Gerais. Av. Presidente Antônio Carlos, 6627, Belo Horizonte, Minas Gerais, Brazil. 31270-901. E-mail: silviafsousa@yahoo.com.br; silviafsousa@ufmg.br

Abstract

Objective: Sjögren disease (SD) is marked by salivary gland fibrosis, which can be evaluated using shear wave elastography (SWE), an ultrasound-based method for quantifying tissue stiffness. Our aim was twofold: to propose a standardized SWE protocol for major salivary glands and to review and meta-analyze its diagnostic performance in SD classified by the 2016 ACR/EULAR criteria.

Materials and Methods: A pilot protocol was applied to nine age-matched women (three with SD, three with non-SD *sicca*, and three healthy controls), with SWE performed bilaterally in longitudinal and transverse planes. Searches were undertaken in six databases, supplemented by manual scrutiny/gray literature. Cross-sectional and diagnostic accuracy studies were included. Risk of bias was appraised using the Joanna Briggs Institute tool.

Results: The series showed SWE measurement variability across regions and planes, highlighting the need for comprehensive assessment to detect focal/asymmetric involvement. Eleven studies comprising 1,029 individuals (530 with SD, 499 controls; female-to-male ratio 15.2:1) were included. Meta-analyses showed significantly higher SWE values in SD patients, with parotid elastography demonstrating greater diagnostic accuracy than submandibular (82.9% *vs*. 73.1%).

Conclusion: SWE effectively differentiates SD from healthy controls, particularly when assessing the parotid gland. Standardization of SWE protocols may enhance diagnostic accuracy and foster clinical integration.

Keywords: autoimmune diseases; elastography; salivary glands; Sjögren disease; ultrasonography.

1. Introduction

Sjögren disease (SD) is a systemic autoimmune condition characterized by chronic lymphocytic infiltration and progressive dysfunction of exocrine glands, primarily affecting salivary and lacrimal tissues (Mariette & Criswell, 2018; Trevisani et al., 2019; Baldini et al., 2024). Besides *sicca* symptoms, the disease may exhibit heterogeneous systemic manifestations that may include musculoskeletal, pulmonary, renal, and neurologic complications (Trevisani et al., 2022; Trevisani et al., 2022; de Oliveira et al., 2025). The shift from "Sjögren's syndrome" to "Sjögren disease" has gained traction in international guidelines, particularly in the recent United Kingdom consensus, which recognizes the condition as a distinct clinical entity with multi-organ involvement (Baer & Hammitt, 2021; Price et al., 2025). Despite an estimated global prevalence ranging from 0.005% to 0.01%, SD remains underdiagnosed, especially in its early stages or in seronegative patients (Beydon et al., 2024).

Salivary gland ultrasonography (SGUS) has gained momentum over the past decade as a non-invasive, accessible, and operator-friendly method for detecting parenchymal changes associated with SD (Jousse-Joulin et al., 2016; van Nimwegen et al., 2020; Manfrè et al., 2021). Its diagnostic performance is promising, particularly when combined with histopathological or serological data. A recent meta-analysis documented pooled sensitivity and specificity values as high as 86% and 87%, respectively (Martins et al., 2024). However, SGUS was not included in the most recent classification criteria of the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) (van Nimwegen et al., 2020; Shiboski et al., 2017). Moreover, substantial heterogeneity in scoring systems, operator dependency, and variability in sonographic interpretation have hindered its full integration into diagnostic algorithms (Martins et al., 2024). These limitations have prompted researchers to explore more objective and quantitative imaging modalities that may complement or surpass SGUS in SD (Bădărînză et al., 2020; Oruk et al., 2021).

Shear wave elastography (SWE), a form of ultrasound elastography, quantifies tissue stiffness in real time and is operator-independent. It has already been validated in clinical protocols for liver fibrosis (Leong et al., 2023), breast cancer (Park & Kang, 2021), and thyroid nodules (Filho et al., 2020). In SD, where glandular fibrosis is a progressive hallmark, SWE represents a robust method for its assessment. It has been suggested that increased stiffness of the major salivary glands correlates with disease

severity, and SWE may enhance diagnostic accuracy even in early stages of SD (Liu et al., 2024). A recent meta-analysis of SWE reported pooled sensitivity and specificity values of 80% and 87%, respectively, with stronger performance observed in younger patients and when both the parotid and submandibular glands were assessed (Dai et al., 2024). Similarly, the application of SWE to lacrimal glands yielded an area under the receiver operating characteristic (ROC) curve of 0.97, indicating excellent discriminatory power (Zhang et al., 2024). Nevertheless, no consensus exists regarding optimal cutoff values, acquisition techniques, or standardization protocols, and many published studies do not strictly adhere to the 2016 ACR/EULAR classification criteria (van Nimwegen et al., 2020; Shiboski et al., 2017), thereby limiting their clinical applicability. Current literature also lacks standardization in the execution of SWE for major salivary glands in SD patients, with substantial heterogeneity in techniques, measurement parameters, and protocols across studies (Karadeniz et al., 2023).

The purpose of the present study was twofold: (i) to propose a standardized and reproducible protocol for the application of SWE in SD screening; and (ii) to systematically review and meta-analyze the diagnostic performance of SWE applied to the major salivary glands in SD, based on studies aligned with the 2016 ACR/EULAR classification criteria.

2. Materials and Methods

2.1 Proposed protocol for exam standardization

2.1.1 Study design, setting, and ethical clearance

This pilot methodological study was conducted using a convenience sample of individuals treated at the School of Dentistry, Universidade Federal de Minas Gerais, in Belo Horizonte, Brazil. All procedures were caried out in December 2024. Ethical approval was obtained from the institution’s Research Ethics Committee (No. 60804622.9.0000.5149). The study complied with the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants.

2.1.2 Participants and eligibility criteria

Nine adult women (median age: 47 years; range: 43–49 years) were age-matched and evenly allocated to three groups: SD, non-SD *sicca*, and healthy controls. Patients with SD were classified according to the most recent ACR/EULAR

classification criteria (Shiboski et al., 2017). Individuals presenting with dry eye and/or dry mouth (xerostomia and/or hyposalivation) who did not meet the ACR/EULAR criteria were categorized as non-SD *sicca* (de Oliveira et al., 2022). The healthy control group comprised individuals without systemic conditions who were receiving dental care at the university. Exclusion criteria were the presence of other concomitant inflammatory rheumatic diseases (e.g., IgG4-related disease), coexisting conditions (e.g., HIV, hepatitis C, amyloidosis, graft-versus-host disease), habits (e.g., smoking and/or alcohol consumption), prior radiotherapy, pregnancy, history of sialolithiasis, parotid duct stenosis, or major salivary gland tumors.

2.1.3 SWE assessment

Ultrasonographic evaluation of the parotid and submandibular glands was performed using a high-frequency linear transducer (3–12 MHz) on a LOGIQ P8 ultrasound system (GE Healthcare™, NY, USA). All procedures were conducted by a dentist (B.L.S.F.) who had been previously calibrated in ultrasonographic techniques. The elastographic measurements were subsequently reviewed and confirmed by a senior oral and maxillofacial radiologist (M.A.A.C.), who was blinded to the participants' group assignments.

The examinations were performed with the patient in the supine position, applying minimal pressure with the transducer while the patient held her breath for a few seconds to reduce motion artifacts. SWE was performed bilaterally in both longitudinal and transverse planes, with measurements obtained from six regions of interest (ROI) per gland. Each ROI value corresponded to the median of 10 measurements automatically acquired by the system within the region. According to the manufacturer, if the variation among these measurements exceeds 35%, the assessment should be repeated. SWE values were recorded in both kilopascals (kPa) and meters per second (m/s).

For the assessment of the submandibular gland in the longitudinal plane, the transducer was positioned parallel to the body of the mandible **(Figure 1A)**. B-mode imaging was initially used to delineate the anteroposterior extension of the glandular parenchyma, and three reference points were marked on the skin to ensure standardized probe placement: anterior, posterior, and midpoint between the anterior and posterior borders of the gland. With the probe still in the longitudinal position, three regions were evaluated in each gland: medial (near the vertex of the submandibular

triangle), intermediate, and lateral (adjacent to the submandibular fossa). For transverse plane assessments, the reference points established during the preceding longitudinal scan were used to guide transducer positioning **(Figure 2A)**. The submandibular gland was then evaluated in its anterior, intermediate, and posterior regions.

Following the same criteria, the parotid gland was assessed in its anterior, intermediate, and posterior regions in the longitudinal plane **(Figure 3A)**, and in its superior, intermediate, and inferior regions in the transverse plane **(Figure 4A)**. To enhance measurement accuracy, all elastographic assessments were performed with careful and consistent transducer pressure, and patients were instructed to remain still and silent throughout the procedure.

2.1.4 Data analysis

Data were tabulated using Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, USA) and analyzed descriptively with GraphPad Prism, version 8.0.0 for Windows (GraphPad Software, San Diego, CA, USA).

2.2 Systematic review

2.2.1 Research question and eligibility criteria

The clinical framework (PIRD question) applied was: What is the contribution of elastography to the diagnosis of individuals with SD or non-SD *sicca*? The components of the framework were defined as follows: P (Patients): individuals with SD or non-SD *sicca*; I (Index test): SWE; R (Reference test): other diagnostic tests or the absence of a comparator; D (Diagnosis): SD or non-SD *sicca*, diagnosed with an analysis of changes in major salivary glands.

Studies using SWE or its variations (e.g., acoustic radiation force impulse [ARFI]) to assess changes in the major salivary glands of individuals with SD or non-SD *sicca* were included. Eligible study designs were diagnostic test accuracy studies. Cross-sectional studies, case-control studies, and clinical trials were also eligible. Exclusion criteria were laboratory-based research (e.g., animal experiments), review articles, letters to the editor, expert opinions, conference/meeting abstracts, and studies that did not adhere to the diagnostic criteria established by the 2016 ACR/EULAR classification (Shiboski et al., 2017).

2.2.2 Databases and search strategies

Electronic searches were conducted across the following databases from their inception to January 2025: PubMed (National Library of Medicine), Web of Science (Clarivate Analytics), Scopus (Elsevier), Embase (Elsevier), Ovid (Wolters Kluwer), and LILACS (Latin American and Caribbean Health Sciences Literature). No restrictions were applied regarding language, publication date, or geographic region. Boolean operators were used to refine the search strategies, with adjustments made to accommodate the specific syntax of each database **(Supplementary File 1)**. Additionally, manual searches of reference lists from the included articles and gray literature searches through Google Scholar (limited to the first 200 records) were performed (Haddaway et al., 2015). Duplicate records across databases were identified and removed using the Rayyan platform (Ouzzani et al., 2016).

2.2.3 Study selection

References retrieved through electronic searches were screened according to the predefined eligibility criteria. Three independent authors (B.L.S.F., L.S.J., and A.C.C.P.) conducted the screening in two distinct phases. In the first phase, titles and abstracts were evaluated and those that appeared to meet the eligibility criteria were submitted to an additional evaluation in the next stage. When titles and abstracts lacked sufficient information, the full text was assessed. In the second phase, whose full text met the eligibility criteria, were included. For studies without full texts, attempts were made to obtain them by contacting the corresponding authors via electronic message (e-mail). Any disagreements among the three authors regarding study selection were resolved through discussion and consensus with the involvement of a fourth author (S.F.S.).

2.2.4 Data coding and extraction

The following data were extracted from each included study: author name(s) and year of publication, country of study, sample size, participant demographic characteristics (age and sex), salivary gland analyzed, plane of analysis, and SWE values reported in m/s and/or kPa. Clinical characteristics of participants with SD, including disease duration, disease activity, focus score, xerostomia, salivary flow, xerophthalmia, and Schirmer test results, were also recorded. Information on

serological parameters, including anti-SSA/Ro, anti-SSB/La, rheumatoid factor, and antinuclear antibodies, was extracted as well.

2.2.5 Critical appraisal

The methodological quality of the included studies was independently assessed by two authors (L.S.J. and S.F.S.) using the Joanna Briggs Institute (JBI) tools for diagnostic test accuracy studies (Campbell et al., 2020) and cross-sectional studies (Moola et al., 2020). Each item in the appraisal tools was rated as “yes” (low risk of bias), “no” (high risk of bias), “unclear” (uncertain risk of bias), or “not applicable”. Any disagreements between the authors were resolved through consensus.

2.2.6 Synthesis of results

Data from homogeneous studies, i.e., those reporting accuracy measures for the same salivary gland and using the same measurement parameters, were pooled for analysis. Meta-analyses comparing elastography mean values and standard deviations between individuals with SD and controls were conducted using Review Manager (RevMan), version 5.4 (The Cochrane Collaboration, Copenhagen, 2020). For studies reporting median and interquartile range (IQR 25%-75%) instead of mean and standard deviations, conversions were performed using the equations proposed by Wan et al. (2014). Additionally, meta-analyses assessing the diagnostic accuracy (area under the curve [AUC]) of elastography in screening for SD were carried out using MedCalc software, version 19.2.6 (MedCalc Software bv, Ostend, Belgium; https://www.medcalc.org, 2020). All meta-analyses employed a random-effect model and heterogeneity was assessed using the I^2. Results were reported as mean difference (MD), 95% confidence interval (CI), and AUC.

2.2.7 Protocol and registration

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42024546909.

3. Results

3.1 Case series

This series evaluated SWE in different regions of the submandibular and parotid glands in nine female patients, aiming to identify variations related to the examination plane (longitudinal or transverse), gland region, and patient group.

In the longitudinal evaluation of the right submandibular gland (Figure 1B), the highest stiffness values on the right side were observed in healthy controls in the lateral region (14.14 kPa), in patients with SD in the intermediate region (12.59 kPa), and in *sicca* patients in the medial region (11.67 kPa). On the left side, *sicca* patients showed the highest values in the lateral (9.76 kPa) and medial regions (11.73 kPa), while healthy controls exhibited the highest stiffness in the intermediate region (9.11 kPa). Stiffness values expressed in m/s followed a similar trend but showed less distinction among groups (Figure 1C).

In the transverse plane (**Figure 2B**), healthy controls exhibited the highest stiffness in the posterior region of the right submandibular gland (11.59 kPa), while *sicca* patients had the highest values on the left (9.12 kPa). In the intermediate region, healthy controls had the highest stiffness on the left (10.38 kPa), whereas *sicca* patients had the highest values on the right (11.00 kPa). In the anterior region, the highest value on the right was found in patients with SD (13.42 kPa), while on the left it was markedly higher in *sicca* patients (14.45 kPa) (**Figure 2C**).

For the parotid glands (**Figure 3B**), the highest stiffness in the posterior region was found in patients with SD on the right (10.43 kPa) and in healthy controls on the left (12.81 kPa). In the intermediate region, patients with SD exhibited the highest value on the left (21.62 kPa), while healthy controls had the highest value on the right (12.77 kPa). In the anterior region, healthy controls demonstrated the highest stiffness bilaterally (14.35 kPa right, 12.99 kPa left) (**Figure 3C**). In the superior region of the parotid gland (**Figure 4B**), patients with SD had the highest stiffness on both sides (11.38 kPa right, 11.93 kPa left). In the intermediate region, stiffness was highest in patients with SD on the left (16.55 kPa) and in healthy controls on the right (12.51 kPa). In the inferior region, healthy controls had the highest values on the right (9.62 kPa), while patients with SD had the highest on the left (10.04 kPa) (**Figure 4C**).

3.2 Systematic review

3.2.1 Literature search and geographic distribution

The electronic search yielded 162 articles. After the removal of 87 duplicates, 75 references were screened for eligibility and 10 articles were included. Additionally, one article meeting the eligibility criteria was identified through manual searches/gray literature sources. Thus, 11 articles were included in the final analysis. These comprised 10 cross-sectional studies (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Caraba et al., 2019; Özer et al., 2023; Prata et al., 2022; Satış et al., 2020; Świecka et al., 2022; Turnaoglu et al., 2018; Xu et al., 2023) and one diagnostic test accuracy study (Güngör et al., 2022). **Supplementary File 2** presents the flowchart outlining the article selection process. The studies were published between 2018 (Turnaoglu et al., 2018) and 2023 (Xu et al., 2023) and were from Turkey (Karadeniz et al., 2023; Arslan et al., 2020; Güngör et al., 2022; Özer et al., 2023; Satış et al., 2020; Turnaoglu et al., 2018), Romania (Bădărînză et al., 2020; Caraba et al., 2019), Poland (Świecka et al., 2022), Portugal (Prata et al., 2022), and China (Xu et al., 2023).

3.2.2 Clinicodemographic aspects

A total of 1,029 individuals were analyzed, of whom 933 (90.67%) were female and 61 (5.92%) were male, resulting in a female-to-male ratio of 15.2:1. One study did not report the sex distribution of participants (*n*=35) (Bădărînză et al., 2020). Among the total sample, 530 (51.5%) individuals were diagnosed with SD, while 499 (48.5%) served as healthy controls. The mean age of patients with SD ranged from 49 to 57 years, whereas in healthy participants, age ranged from 33.9 to 55 years.

Sample sizes across the studies ranged from 47 to 186 participants. Eight studies included a balanced number of individuals with SD and healthy controls (Arslan et al., 2020; Bădărînză et al., 2020; Caraba et al., 2019; Güngör et al., 2022; Özer et al., 2023; Satış et al., 2020; Turnaoglu et al., 2018; Xu et al., 2023). Two studies had a higher proportion of patients with SD compared to healthy controls (2:1) (Karadeniz et al., 2023; Prata et al., 2022), whereas one study included more healthy individuals than patients with SD (2.4:1) (Świecka et al., 2022). In seven studies, the control groups were matched for age and sex (Bădărînză et al., 2020; Karadeniz et al., 2023; Güngör et al., 2022; Özer et al., 2023; Prata et al., 2022; Satış et al., 2020; Xu et al., 2023) and one also matched participants by body mass index (Bădărînză et al., 2020) (Table 1).

The mean duration of SD ranged from 34 months to over 96 months. Clinical disease activity values were reported in only two studies: Karadeniz et al. (2023) assessed activity using the EULAR Sjögren's Syndrome Patient-Reported Index (ESSPRI), while Özer et al. (2023) used the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (Table 2).

3.2.3 ACR/EULAR 2016 classification criteria

The focus score was reported in four studies (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Özer et al., 2023), with two of them documenting a focus score ≥1 in most patients (Bădărînză et al., 2020; Karadeniz et al., 2023). Xerostomia and xerophthalmia were reported in more than 60% of individuals across the included studies (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Güngör et al., 2022; Özer et al., 2023; Prata et al., 2022; Satış et al., 2020; Turnaoglu et al., 2018). The mean salivary flow rate was documented in only one study (Caraba et al., 2019). Seven studies reported Schirmer test results, with positivity rates ranging from 37.5% to 100% of patients (Karadeniz et al., 2023; Caraba et al., 2019; Güngör et al., 2022; Özer et al., 2023; Prata et al., 2022; Turnaoglu et al., 2018). Additional correlations between clinical parameters and SWE findings are detailed in **Supplementary File 3**.

Anti-SSA antibodies were detected in 36% to 100% of participants (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Caraba et al., 2019; Güngör et al., 2022; Özer et al., 2023; Prata et al., 2022; Satış et al., 2020; Turnaoglu et al., 2018; Xu et al., 2023). Anti-SSB autoantibodies were positive in 16% to 100% of patients analyzed (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Caraba et al., 2019; Özer et al., 2023; Prata et al., 2022; Turnaoglu et al., 2018). Rheumatoid factor was positive in 24% to 100% of cases (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Caraba et al., 2019; Özer et al., 2022; Turnaoglu et al., 2018). Anti-nuclear antibodies were positive in 60.9% to 100% of patients (Karadeniz et al., 2023; Arslan et al., 2020; Caraba et al., 2019; Özer et al., 2022; Satış et al., 2020; Turnaoglu et al., 2018).

3.2.4 SWE results

Table 1 presents a comparison of the SWE examinations conducted in the included studies, while **Supplementary File 4** details the technical aspects of SWE. In

seven studies, SWE was performed with fewer than five measurements (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Güngör et al., 2022; Özer et al., 2023; Satış et al., 2020; Xu et al., 2023), whereas only one study performed 10 measurements (Turnaoglu et al., 2018). Additionally, one study compared two different SWE techniques at the same ROI, using both one and four measurements (Güngör et al., 2022). Through longitudinal and/or transverse plane analyses, both the parotid and submandibular salivary glands were evaluated in 10 studies (Bădărînză et al., 2020; Arslan et al., 2020; Caraba et al., 2019; Güngör et al., 2022; Özer et al., 2023; Prata et al., 2022; Satış et al., 2020; Swiecka et al., 2022; Turnaoglu et al., 2018; Xu et al., 2023), whereas only one study (Karadeniz et al., 2023) focused exclusively on the parotid gland. Eight studies assessed a single region of the gland (Bădărînză et al., 2020; Karadeniz et al., 2023; Arslan et al., 2020; Güngör et al., 2022; Satış et al., 2020; Świecka et al., 2022; Turnaoglu et al., 2018; Xu et al., 2023), one study evaluated three regions (Caraba et al., 2019), another examined two or more regions (Özer et al., 2023), and one study assessed six distinct regions of the gland (Prata et al., 2022).

Elastography results were expressed in both m/s and kPa in four studies (Arslan et al., 2020; Özer et al., 2023; Satış et al., 2020; Xu et al., 2023). The remaining seven studies reported values exclusively in either m/s (Caraba et al., 2019; Prata et al., 2022; Turnaoglu et al., 2018) or kPa (Bădărînză et al., 2020; Karadeniz et al., 2023; Güngör et al., 2022; Świecka et al., 2022). Among patients with SD, the mean tissue stiffness ranged from 1.71 to 3.4 m/s, whereas in healthy controls, it ranged from 1.59 to 2.3 m/s. Mean elasticity values expressed in kPa ranged from 8.05 to 37.9 kPa in patients with SD and from 5.39 to 18.3 kPa in the control group.

3.2.5 SWE and clinical parameters

The association between SWE values of the salivary glands and clinical parameters in individuals with SD was evaluated in seven studies (Bădărînză et al., 2020; Caraba et al., 2019; Güngör et al., 2022; Karadeniz et al., 2023; Özer et al., 2023; Świecka et al., 2022; Turnaoglu et al., 2018). Higher SWE values were associated with salivary flow (1/1) (Caraba et al., 2019), parotid gland enlargement (1/1) (Bădărînză et al., 2020), Schirmer test results (1/2) (Karadeniz et al., 2023), focus score (1/3) (Caraba et al., 2019), ANA titers (1/3) (Świecka et al., 2022), rheumatoid factor (2/4) (Bădărînză et al., 2020; Świecka et al., 2022), beta-2 microglobulin serum concentration (1/1) (Caraba et al., 2019), gamma globulin levels (1/1) (Świecka et al.,

2022), and C3/C4 complement concentrations (1/3) (Bădărînză et al., 2020). No significant associations were found between SWE values and age (Karadeniz et al., 2023; Özer et al., 2023), disease duration (Güngör et al., 2022; Karadeniz et al., 2023; Özer et al., 2023; Turnaoglu et al., 2018), disease activity (Karadeniz et al., 2023; Özer et al., 2023), xerostomia (Karadeniz et al., 2023; Turnaoglu et al., 2018), xerophthalmia (Karadeniz et al., 2023), or anti-SSA and anti-SSB antibodies (Bădărînză et al., 2020; Karadeniz et al., 2023; Özer et al., 2023).

3.2.6 SWE and SGUS grading systems

Five studies compared mean SWE values in relation to SGUS grading systems (Karadeniz et al., 2023; Arslan et al., 2020; Özer et al., 2023; Caraba et al., 2019; Prata et al., 2022). An increase in SWE values corresponding to higher SGUS grades in the salivary glands was observed in two studies (Arslan et al., 2020; Özer et al., 2023). A positive correlation between B-mode scoring and SWE measurements in m/s was also reported (Caraba et al., 2019; Prata et al., 2022). One study (Prata et al., 2022) found that the combination of SWE and SGUS provided excellent diagnostic performance in distinguishing patients with SD from controls. Also, when analyzed separately, SWE outperformed B-mode in classifying individuals with SD (Karadeniz et al., 2023).

3.2.7 SWE quantitative synthesis

Two meta-analyses demonstrated that the elastography values (m/s) of the parotid gland in individuals with SD were significantly higher than those in controls (MD=0.78 m/s, [95% CI: 0.54–1.02], I^2=95.0%) (**Figure 5A**). Similarly, elastography values (m/s) of the submandibular gland were significantly higher in patients with SD compared to controls (MD=0.48 m/s, [95% CI: 0.33–0.63], I^2=91.0%) (**Figure 5B**). Two additional meta-analyses revealed significantly higher elastography values (kPa) in the parotid gland of individuals with SD than in controls (MD=12.37 kPa, [95% CI:8.65–16.10], I^2=96.0%) (**Figure 5C**). The elastography values (kPa) in the submandibular glands were significantly elevated in patients with SD compared to controls (MD=9.09 kPa, [95% CI:4.88–13.31], I^2=97.0%) (**Figure 5D**).

ROC analysis was conducted in seven of the 11 included studies to assess the diagnostic performance of SWE. Two meta-analyses revealed that the accuracy of parotid elastography (kPa) for screening individuals with SD was 82.9% (AUC=82.9%, [95% CI: 68.9%-96.9%], I^2=92.0%) (**Figure 6A**). The accuracy of parotid elastography

measured in m/s was 73.1% (AUC=73.1%, [95% CI: 61.5%-84.8%], I^2=80.8%) (**Figure 6B**). For the submandibular gland, the accuracy of elastography in kPa was 65.7% (AUC=65.7%, [95% CI: 57.7%-73.7%], I^2=0.0%) (**Figure 6C**), while elastography in m/s yielded an accuracy of 66.5% (AUC=66.5%, [95% CI: 59.2%-73.8%], I^2=0.0%) (**Figure 6D**).

3.2.8 Critical appraisal

The diagnostic accuracy study exhibited limitations related to its design and to the reference standard's ability to correctly classify the target condition (**Supplementary File 5**). Among the cross-sectional studies, 100% clearly defined inclusion criteria, described the study setting in detail, used valid and reliable methods to measure exposure and outcomes, and applied standardized diagnostic criteria. However, only 60% identified confounding factors and 80% performed appropriate statistical analyses (**Supplementary File 6**).

4. Discussion

The present study demonstrated that SWE values were significantly higher in individuals with SD compared to healthy controls, particularly in the parotid gland. SWE measurements in the parotid consistently outperformed those in the submandibular gland, reinforcing its diagnostic utility. These findings support the use of SWE as a valuable, non-invasive imaging modality for detecting glandular changes in SD and underscore the parotid gland as a reliable target in elastographic assessments. However, variability in SWE measurements across regions and imaging planes of the major salivary glands emphasizes the need for protocol standardization.

SWE is a modern ultrasound-based technique that quantifies tissue stiffness by measuring the speed of shear wave propagation (Cosgrove et al., 2013; Chen et al., 2016). In SD, glandular fibrosis and acinar atrophy likely account for the increased stiffness, lending biological plausibility to SWE-derived metrics. Previous studies have applied SWE to differentiate individuals with SD from healthy controls (Wierzbicka et al., 2014; Hofauer et al., 2016; Cindil et al., 2018), to correlate stiffness with B-mode ultrasound abnormalities (Prata et al., 2022), and to evaluate its diagnostic performance (Arslan et al., 2020). Although several imaging studies support the role of SWE in detecting salivary gland involvement in SD (Bădărînză et al., 2020; Caraba et al., 2019; Güngör et al., 2022; Karadeniz et al., 2023; Özer et al., 2023; Świecka et al.,

2022; Turnaoglu et al., 2018), its association with clinical and laboratory parameters remains inconclusive. In this review, only six studies explored these associations, and few reported meaningful correlations (Caraba et al., 2019; Świecka et al., 2022). For instance, since the reported agreement between labial salivary gland biopsy and parotid gland findings (Wise et al., 1988; Mossel et al., 2017), and that glandular stiffness is likely influenced by the degree of inflammation, this relationship with SWE-derived quantitative data remains to be defined.

Unstimulated salivary flow, a component of the diagnostic criteria for SD (Shiboski et al., 2017), can vary in severity (Proctor & Shaalan, 2021). We found that only one study reported the mean value of saliva collected (Caraba et al., 2019) and examined its association with SWE findings. Conversely, SWE values did not correlate with xerostomia, ESSDAI, ESSPRI, or anti-SSA/SSB positivity. This apparent dissociation between local tissue stiffness and systemic markers may reflect the heterogeneous pathophysiological mechanisms underlying SD, in which focal glandular inflammation and fibrosis do not always parallel systemic immune activation or symptom severity (Ma et al., 2024). Moreover, subjective symptoms such as dryness are multifactorial and may persist despite histological or immunological remission, limiting their value as correlations of imaging findings (Zandonella Callegher et al., 2022).

Age-related factors critically influence SWE interpretation. Most studies included in this review adjusted for age and sex (Badarinza et al., 2020; Prata et al., 2022; Xu et al., 2023), and at least one accounted for body mass index (Badarinza et al., 2020). This methodological rigor is essential, given that salivary gland function naturally declines with age—even in healthy individuals—potentially confounding SWE measurements (Oxholm, 1992). A recent post-mortem study revealed compelling morphological evidence of age-related degeneration in the minor salivary glands of women, including acinar atrophy, serous metaplasia, fibrosis, and ductal ectasia, i.e., changes that were more pronounced after menopause (de Moraes et al., 2024). These findings support the idea that structural remodeling due to aging may compromise glandular tissue elasticity, thereby affecting SWE readings irrespective of disease status. Although the mean age of SD cohorts in SWE studies ranged from 49 to 57 years, aligning with the peak incidence of SD (Xu et al., 2023), no significant association between SWE values and age was found elsewhere (Karadeniz et al., 2023; Özer et al., 2023). However, a recent meta-analysis indicated that SWE performs

better in patients aged ≤51 years (Dai et al., 2024). These observations suggest that age-stratified SWE thresholds may be necessary to optimize diagnostic accuracy.

Disease duration also failed to correlate with SWE values in four studies (Güngör et al., 2022; Karadeniz et al., 2023; Özer et al., 2023; Turnaoglu et al., 2018), likely reflecting the insidious onset and subclinical progression of SD (Oxholm et al., 1992). Martins et al. (2024) reinforced the notion that imaging parameters may more accurately reflect glandular pathology than chronological disease metrics. Accordingly, ultrasonography may detect ongoing glandular remodeling independently of clinical duration, positioning SWE as a dynamic tool for monitoring disease progression or therapeutic response (Martins et al., 2024; Inanç et al., 2019; Finzel et al., 2021; Carotti et al., 2014). From this perspective, we hypothesize that SWE could be particularly useful in identifying subclinical glandular changes in early-stage or seronegative SD; an assertion that warrants validation in longitudinal cohorts.

Integrating SWE with B-mode ultrasound has emerged as a promising diagnostic strategy. B-mode scoring systems detect echotextural changes, such as inhomogeneity and hypoechogenicity, which reflect disease progression (Lee et al., 2020; Chen et al., 2023). Nevertheless, SWE can reveal stiffness abnormalities even in morphologically normal glands, thereby increasing sensitivity (Bădărînză et al., 2020). Five studies in this review correlated B-mode scores with SWE values (Arslan et al., 2020; Caraba et al., 2019; Özer et al., 2023; Prata et al., 2022; Karadeniz et al., 2023), all demonstrating that increased echostructural damage was associated with higher stiffness. Despite these advantages, heterogeneity among B-mode scoring systems, many of which rely on outdated frameworks such as those proposed elsewhere (Hocevar et al., 2005; Makula et al., 1996), which vary in criteria and thresholds, complicate inter-study comparisons. Interestingly, the validated OMERACT system, which offers improved reproducibility and interobserver agreement (Finzel et al., 2021), was not applied in any of the studies included in the current review, highlighting a methodological gap that hinders broader applicability and consensus.

Regarding technical aspects, two SWE modalities were represented: acoustic radiation force impulse imaging (ARFI) (Caraba et al., 2019; Turnaoglu et al., 2018) and the more advanced 2D-SWE (Arslan et al., 2020; Badarinza et al., 2020; Güngör et al., 2022; Karadeniz et al., 2023; Prata et al., 2022; Özer et al., 2023; Satış et al., 2020; Świecka et al., 2022; Xu et al., 2023), with the latter offering broader tissue sampling and superior reproducibility (Prata et al., 2022). Results were expressed in

both kPa and m/s, although these metrics are not directly interchangeable. While kPa values may be more affected by tissue heterogeneity (Alfuraih et al., 2018), our meta-analysis revealed higher diagnostic accuracy in kPa than in m/s, particularly in the parotid gland (82.9% *vs*. 73.1%). This finding supports previous reports suggesting that the parotid gland is more frequently and severely affected in SD (Arslan et al., 2020; Prata et al., 2022). Nonetheless, bilateral evaluation remains essential, as side-to-side asymmetry in SWE values is not uncommon (Jousse-Joulin & Coiffier, 2020), and unilateral alterations may indicate alternative diagnoses. A former meta-analysis showed that when SWE was performed on both the parotid and submandibular glands, the specificity reached 96% for correctly identifying non-SD patients (Dai et al., 2024).

Our experience underscores the need to standardize SWE for the detection of SD. We performed SWE bilaterally, in both longitudinal and transverse planes, acquiring measurements from six ROI per gland. Each ROI value represented the median of 10 measurements automatically acquired by the system. SWE values expressed in kPa and m/s varied across the study groups. Heterogeneous stiffness values were observed in different regions of the parenchyma, in both the parotid and submandibular glands bilaterally. On this basis, limiting SWE to a single gland, region, or imaging plane may obscure disease-related changes, particularly in cases of early or focal involvement. Concerning the imaging plane, the literature showed a tendency for SWE to be performed more frequently in the longitudinal plane (Arslan et al., 2020; Caraba et al., 2019; Güngör et al., 2022; Prata et al., 2022; Özer et al., 2023; Satış et al., 2020; Turnaoglu et al., 2018; Xu et al., 2023). However, no consensus exists for the parotid gland, which was also examined in the transverse plane (Karadeniz et al., 2023; Prata et al., 2022), possibly due to reduced anatomical overlap from structures such as bones, salivary ducts, and vascular branches.

Limitations of the present study should be acknowledged. First, none of the studies included in our review compared SD with non-Sjögren *sicca*, a critical differential diagnosis. Thus, the specificity of SWE in distinguishing SD from other causes of *sicca* remains to be defined. Second, although all studies adopted the 2016 ACR/EULAR classification criteria (Shiboski et al., 2017), none incorporated the OMERACT consensus score (Rebel et al., 2024). Additionally, the therapeutic effects on SWE remain unexplored, although changes in SGUS in response to treatment have been reported in the literature (Fisher et al., 2018; Jousse-Joulin et al., 2015). Although the studies retrieved in this review did not assess SWE before and after treatment, the

technique could be further explored as a safe adjunct for disease monitoring. As far as we know, this is the first systematic review and meta-analysis specifically designed to evaluate studies in which all individuals with SD were classified according to the most recent ACR/EULAR criteria (Shiboski et al., 2017).

5. Conclusion

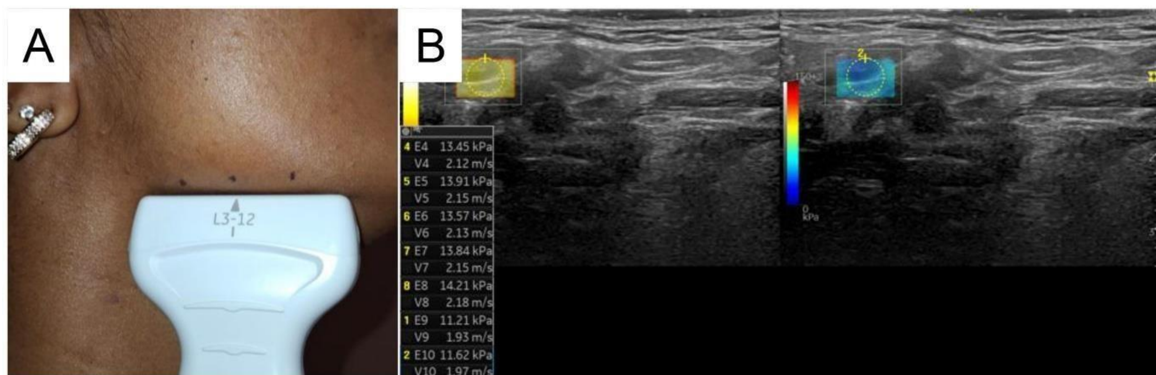
In summary, our findings demonstrated that SWE can effectively differentiate SD from healthy controls, particularly when applied to the parotid gland and interpreted in kPa. Data suggest that SWE provides incremental diagnostic value beyond conventional SGUS and should be further explored as a standardized, non-invasive tool for SD assessment. Future research should prioritize longitudinal analyses, harmonized scoring protocols, and the inclusion of non-Sjögren *sicca* populations to fully elucidate the clinical utility of SWE.

Acknowledgements: The authors thank the financial support from Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG; APQ-03440-22), Pró-Reitoria de Pós-Graduação e de Extensão (PRPG/PROEX), Fundo Fundep – UFMG and Rotary International. We would like to thank Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ; E-26/200.330/2024; E-26/200.331/2024), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES; Finance Code 001), and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; 305077/2021-0).

Conflict of Interest: None to declare.

Source of Funding: None.

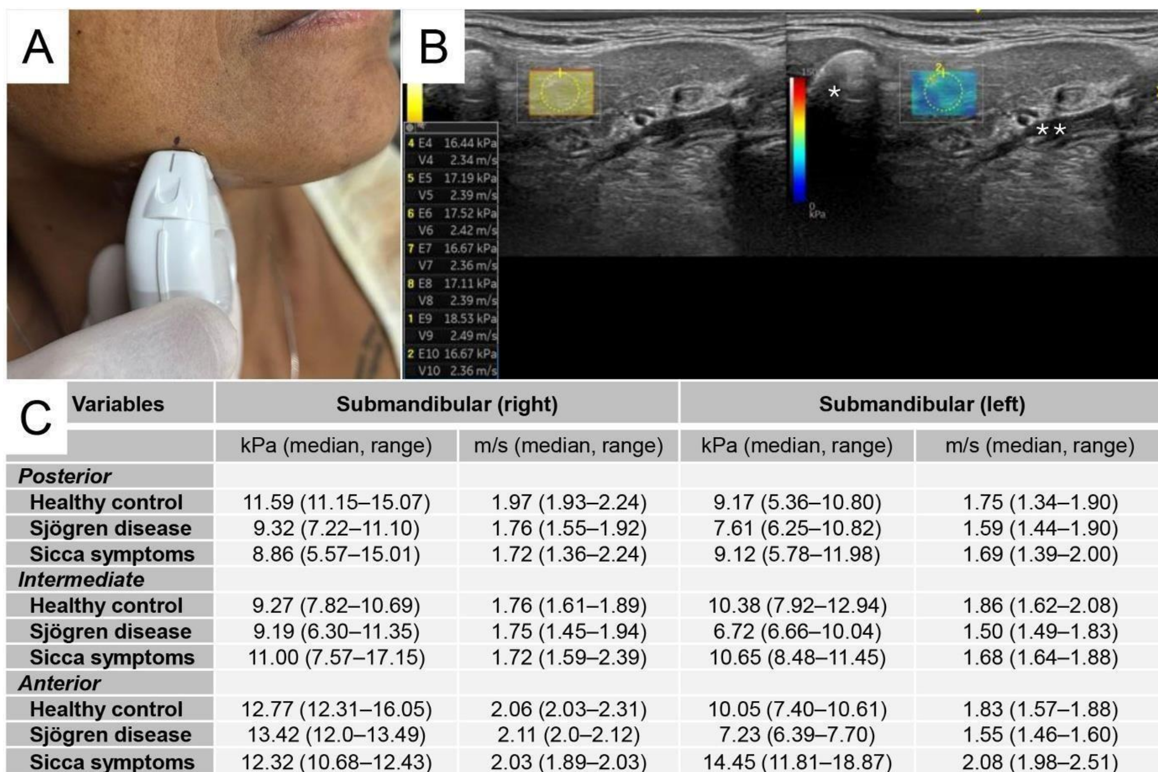
Figure 1. (A) Longitudinal positioning for anteroposterior assessment of the submandibular gland, with the transducer aligned parallel to the mandibular body. **(B)** This positioning allows for the identification of medial, intermediate, and lateral regions for longitudinal shear-wave measurements. **(C)** The table presents shear-wave elastography values, reported in kilopascals (kPa) and meters per second (m/s), for the right and left submandibular glands across different regions (lateral, intermediate, and medial) in healthy controls, individuals with Sjögren disease (SD), and those with non-SD *sicca*.



C

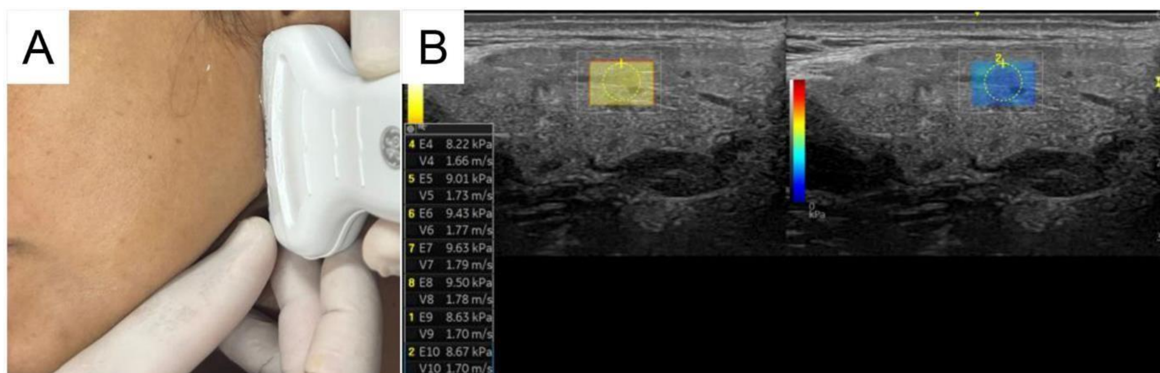
Variables	Submandibular (right)		Submandibular (left)	
	kPa (median, range)	m/s (median, range)	kPa (median, range)	m/s (median, range)
Lateral				
Healthy control	14.14 (13.74–18.76)	2.17 (2.14–2.50)	5.46 (4.55–12.95)	1.35 (1.23–2.08)
Sjögren disease	12.57 (7.77–13.88)	2.05 (1.61–2.15)	6.65 (6.52–9.03)	1.49 (1.47–1.73)
Sicca symptoms	9.85 (8.47–22.07)	1.81 (1.68–2.71)	9.76 (9.32–10.17)	1.80 (1.76–2.03)
Intermediate				
Healthy control	12.95 (4.75–13.67)	2.08 (1.26–2.13)	9.11 (5.12–16.17)	1.74 (1.31–2.32)
Sjögren disease	12.59 (10.89–13.53)	2.05 (1.91–2.12)	8.57 (5.48–11.61)	1.69 (1.35–1.97)
Sicca symptoms	11.12 (10.16–13.05)	1.93 (1.84–2.09)	10.00 (6.70–12.27)	2.02 (1.49–2.02)
Medial				
Healthy control	9.94 (8.69–10.41)	1.82 (1.70–1.86)	10.22 (9.55–17.65)	1.84 (1.78–2.43)
Sjögren disease	11.29 (10.23–12.54)	1.94 (1.85–2.04)	9.74 (8.66–12.55)	1.80 (1.70–2.05)
Sicca symptoms	11.67 (10.94–17.99)	1.97 (1.91–2.45)	11.73 (9.83–21.35)	1.81 (1.67–2.67)

Figure 2. (A, B) Transverse positioning for the assessment of the submandibular gland, with skin markings used as guides for shear-wave measurements in the anterior, intermediate, and posterior regions. **(C)** The table presents shear-wave elastography values, reported in kilopascals (kPa) and meters per second (m/s), for the right and left submandibular glands across different regions in healthy controls, individuals with Sjögren disease (SD), and those with non-SD *sicca*. Note: *mandible; **mylohyoid muscle.



Variables	Submandibular (right)		Submandibular (left)	
	kPa (median, range)	m/s (median, range)	kPa (median, range)	m/s (median, range)
Posterior				
Healthy control	11.59 (11.15–15.07)	1.97 (1.93–2.24)	9.17 (5.36–10.80)	1.75 (1.34–1.90)
Sjögren disease	9.32 (7.22–11.10)	1.76 (1.55–1.92)	7.61 (6.25–10.82)	1.59 (1.44–1.90)
Sicca symptoms	8.86 (5.57–15.01)	1.72 (1.36–2.24)	9.12 (5.78–11.98)	1.69 (1.39–2.00)
Intermediate				
Healthy control	9.27 (7.82–10.69)	1.76 (1.61–1.89)	10.38 (7.92–12.94)	1.86 (1.62–2.08)
Sjögren disease	9.19 (6.30–11.35)	1.75 (1.45–1.94)	6.72 (6.66–10.04)	1.50 (1.49–1.83)
Sicca symptoms	11.00 (7.57–17.15)	1.72 (1.59–2.39)	10.65 (8.48–11.45)	1.68 (1.64–1.88)
Anterior				
Healthy control	12.77 (12.31–16.05)	2.06 (2.03–2.31)	10.05 (7.40–10.61)	1.83 (1.57–1.88)
Sjögren disease	13.42 (12.0–13.49)	2.11 (2.0–2.12)	7.23 (6.39–7.70)	1.55 (1.46–1.60)
Sicca symptoms	12.32 (10.68–12.43)	2.03 (1.89–2.03)	14.45 (11.81–18.87)	2.08 (1.98–2.51)

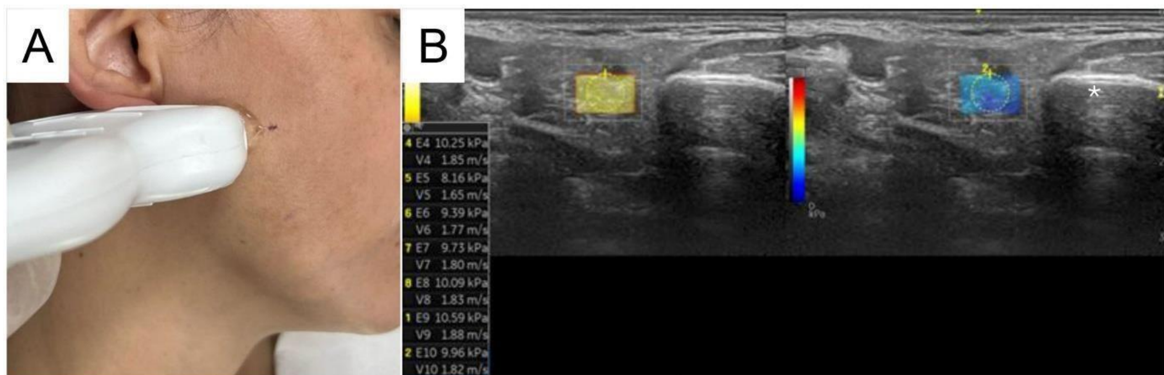
Figure 3. (A) Longitudinal positioning for the assessment of the parotid gland, with one end placed on the mastoid process and the other on the mandibular ramus. **(B)** This positioning facilitates the identification of anterior, intermediate, and posterior regions for longitudinal shear-wave measurements. **(C)** The table presents shear-wave elastography values, reported in kilopascals (kPa) and meters per second (m/s), for the right and left parotid glands across different regions in healthy controls, individuals with Sjögren disease (SD), and those with non-SD *sicca*.



C

Variables	Parotid (right)		Parotid (left)	
	kPa (median, range)	m/s (median, range)	kPa (median, range)	m/s (median, range)
Posterior				
Healthy control	9.96 (8.22–10.46)	1.82 (1.65–1.87)	12.81 (11.95–14.48)	2.07 (2.00–2.20)
Sjögren disease	10.43 (8.95–36.67)	1.86 (1.73–3.50)	10.82 (9.29–49.48)	1.76 (1.42–4.06)
Sicca symptoms	10.67 (8.97–10.85)	1.89 (1.75–1.90)	9.22 (9.06–13.03)	1.75 (1.74–2.08)
Intermediate				
Healthy control	12.77 (9.62–13.69)	2.06 (1.79–2.14)	9.33 (8.01–11.65)	1.76 (1.63–1.97)
Sjögren disease	11.51 (9.22–19.18)	1.96 (1.75–2.53)	21.62 (11.96–49.39)	2.68 (2.00–4.06)
Sicca symptoms	10.00 (8.21–12.67)	1.83 (1.66–2.05)	11.01 (9.79–12.39)	1.92 (1.81–2.03)
Anterior				
Healthy control	14.35 (11.26–15.87)	2.19 (1.94–2.30)	12.99 (9.85–14.10)	2.08 (1.81–2.17)
Sjögren disease	12.71 (8.21–21.40)	2.06 (1.65–2.67)	16.48 (10.96–30.03)	2.34 (1.56–3.16)
Sicca symptoms	10.23 (9.23–12.71)	1.85 (1.74–2.06)	12.70 (12.20–13.10)	2.06 (2.02–2.09)

Figure 4. **(A, B)** Transverse positioning for the assessment of the parotid gland, with skin markings used as guides for shear-wave measurements in the superior, intermediate, and inferior regions. **(C)** The table presents shear-wave elastography values, reported in kilopascals (kPa) and meters per second (m/s), for the right and left parotid glands across different regions in healthy controls, individuals with Sjögren disease (SD), and those with non-SD *sicca*. Note: *mandibular ramus.



C

Variables	Parotid (right)		Parotid (left)	
	kPa (median, range)	m/s (median, range)	kPa (median, range)	m/s (median, range)
Superior				
Healthy control	7.77 (7.34–8.31)	1.61 (1.56–1.66)	10.73 (8.97–14.96)	1.83 (1.79–2.23)
Sjögren disease	11.38 (7.77–13.86)	1.95 (1.61–2.15)	11.93 (8.41–25.03)	1.99 (1.6–2.89)
Sicca symptoms	9.97 (9.21–13.6)	1.82 (1.75–2.13)	9.63 (9.58–13.29)	1.79 (1.79–2.10)
Intermediate				
Healthy control	12.51 (6.35–14.61)	2.04 (1.45–2.21)	10.51 (6.8–10.77)	1.87 (1.51–1.89)
Sjögren disease	11.35 (9.6–14.58)	1.95 (1.79–2.2)	16.55 (10.47–53.85)	2.35 (1.87–3.95)
Sicca symptoms	7.67 (6.95–16.63)	1.6 (1.52–2.35)	8.54 (8.19–9.63)	1.69 (1.65–1.79)
Inferior				
Healthy control	9.62 (7.44–14.11)	1.79 (1.58–2.17)	6.84 (6.55–10.37)	1.51 (1.48–1.86)
Sjögren disease	7.23 (7.07–8.92)	1.55 (1.54–1.72)	10.04 (6.06–13.83)	1.9 (1.83–2.15)
Sicca symptoms	6.18 (4.98–7.49)	1.43 (1.29–1.58)	8.09 (8.05–8.49)	1.64 (1.64–1.68)

Figure 5. Forest plots illustrating the diagnostic accuracy of shear wave elastography (SWE) for screening individuals with Sjögren disease (SD). **(A)** Parotid gland – measured in meters per second (m/s); **(B)** Parotid gland – measured in kilopascals (kPa); **(C)** Submandibular gland – measured in kPa; **(D)** Submandibular gland – measured in m/s.

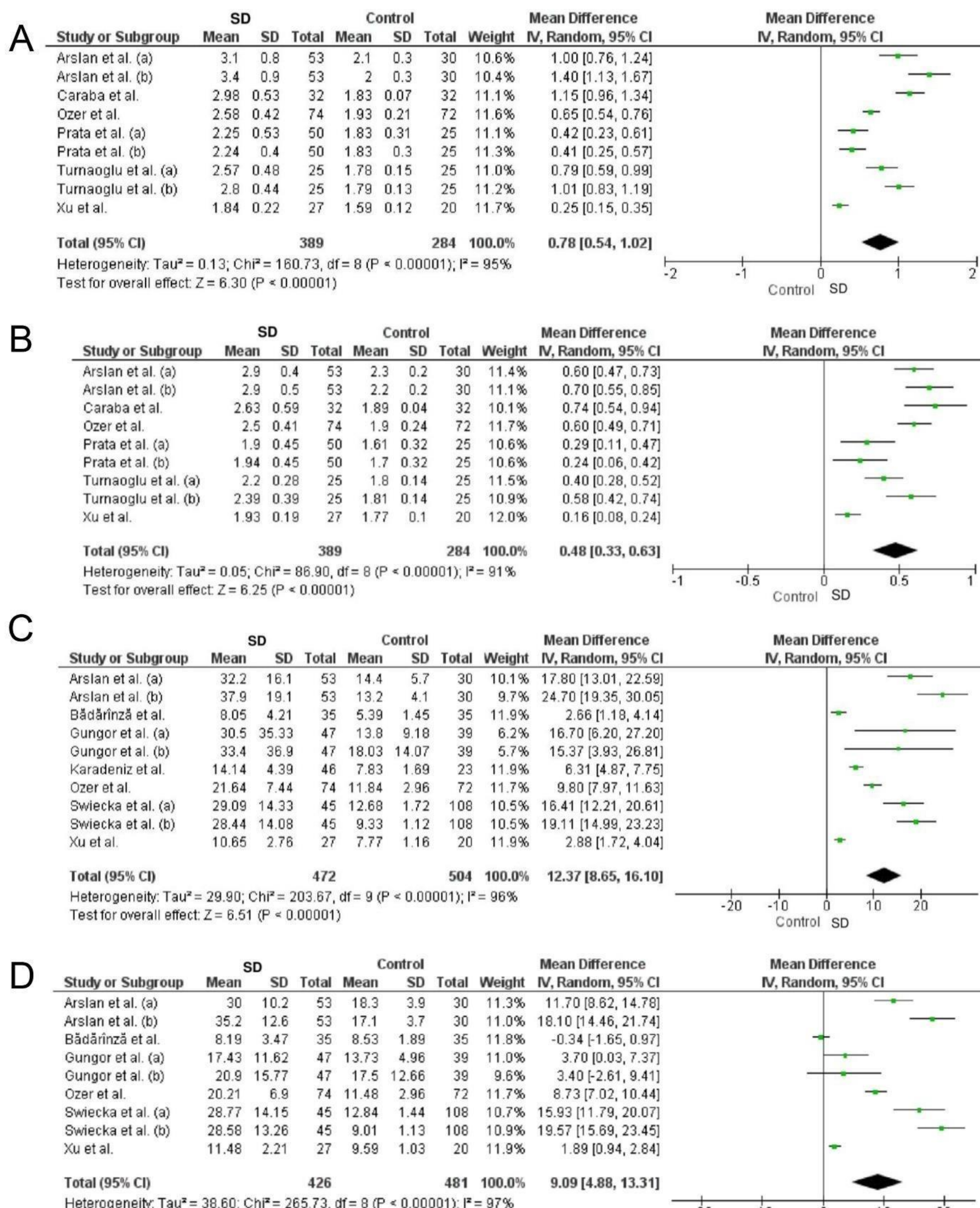


Figure 6. Meta-analyses comparing elastography values between individuals with Sjögren disease (SD) and controls. **(A)** Parotid gland – measured in meters per second (m/s); **(B)** Submandibular gland – measured in m/s; **(C)** Parotid gland – measured in kilopascals (kPa); **(D)** Submandibular gland – measured in kPa.

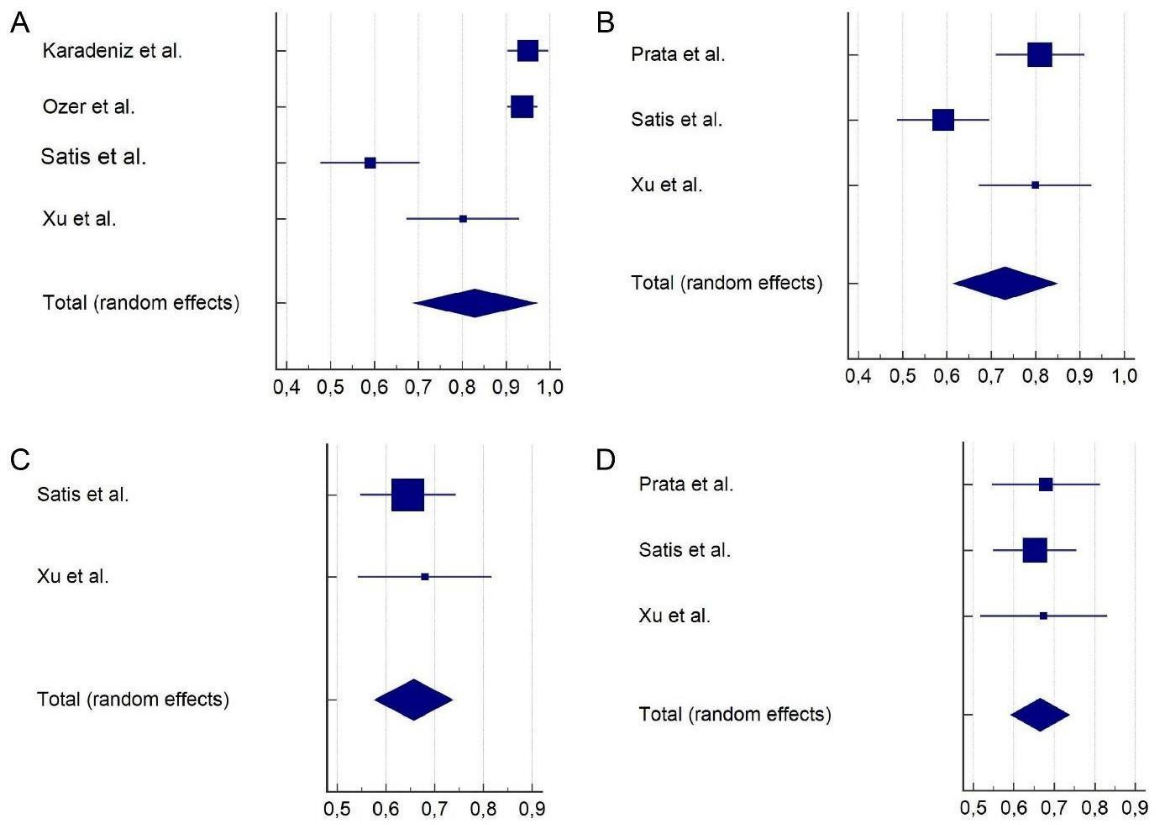


Table 1. Data on studies, demographic characteristics of enrolled patients, and comparison of shear-wave elastography scores (m/s and kPa) between Sjögren disease (SD) and the control group.

Study	Study design	Sample	SD group			Control group			Measures	Salivary gland analyzed (plane of analysis)	SD group	Control group	SD group	Control group
			n	Age (mean)	Sex (F/M)	n	Age (mean)	Sex (F/M)			Shear-wave velocity (m/s)		Elasticity modulus (kPa)	
Arslan *et al.*, 2020; Turkey	Cross-sectional	83	53	49.0	48/5	30	33.9	25/5	1	**Parotid (L)** Right Left **Submandibular (L)** Right Left	3.1 ± 0.8 3.4 ± 0.9 2.9 ± 0.4 2.9 ± 0.5	2.1 ± 0.3 2 ± 0.3 2.3 ± 0,2 2.2 ± 0.2	32.2 ±16.1 37.9 ± 19.1 30 ± 10.2 35.2 ± 12.6	14.4 ± 5.7 13.2 ± 4.1 18.3 ± 3.9 17.1 ± 3.7
Bădărînză *et al.*, 2020; Romania	Cross-sectional	70	35	57.0	33/2	35	NI	NI	3	**Parotid (NI)** **Submandibular (NI)**	-	-	8.05 ± 4.21 8.19 ± 3.47	5.39 ± 1.45 8.53 ± 1.89
Caraba *et al.*, 2019; Romania	Cross-sectional	64	32	52.28	24/8	32	51.78	24/8	6	**Parotid (L)** **Submandibular (L)**	2.98 ± 0.53 2.63 ± 0.59	1.83 ± 0.07 1.89 ± 0.04	-	-
Güngör *et al.*, 2022; Turkey	Diagnostic Test Accuracy	86	47	52.23	47	39	48.97	39	E1: 4 E2: 1	**Parotid (L)** Right Left **Submandibular (L)** Right Left	–	–	E1: 24.20 E2: 24.60 E1: 25.50 E2: 27.70 E1:16.40 E2:15.40 E1: 18.40 E2: 18.70	E1: 12.60 E2: 15.40 E1: 14.90 E2: 14.80 E1:12.50 E2:13.20 E1: 15.20 E2: 14.70
Karadeniz *et al.*, 2023; Turkey	Cross-sectional	69	46	53.5	44/2	23	44.7	21/2	3	**Parotid (T)**	-	-	14.14 ± 4.39	7.83 ± 1.69

Ozer *et al.*, 2023; Turkey	Cross-sectional	146	74	49.73	72/2	72	48.97	70/2	3	**Parotid (L)** **Submandibular (L)**	2.58 ± 0.42 2.50 ± 0.41	1.93 ± 0.21 1.90 ± 0.24	21.64 ± 7.44 20.21 ± 6.90	11.84 ± 2.84 11.48 ± 2.96
Prata *et al.*, 2022; Portugal	Cross-sectional	75	50	56.2	49/1	25	53.5	24/1	6	**Parotid (L + T)** Right Left **Submandibular (L)** Right Left	2.25 ± 0.53 2.24 ± 0.40 1.90 ± 0.45 1.94 ± 0.45	1.83 ± 0.31 1.83 ± 0.30 1.61 ± 0.32 1.70 ± 0.32	–	–
Satis *et al.*, 2020; Turkey	Cross-sectional	186	96	56.5	92/4	90	55.0	86/4	3	**Parotid (T)** **Submandibular (L)**	1.71 1.97	1.70 1.75	10.3 11.0	9.3 9.9
Swiecka *et al.*, 2022; Poland	Cross-sectional	153	45	50.2	41/4	108	51.6	104/4	5	**Parotid (NI)** Right Left **Submandibular (NI)** Right Left	–	–	29.09 ± 14.33 28.44± 14.08 28.77 ± 14.15 28.58 ± 13.26	12.68 ±1.72 9.33 ± 1.12 12.84 ± 1.44 9.01 ± 1.13
Turnaoglu *et al.*, 2018; Turkey	Cross-sectional	50	25	51.6	24/1	25	47.3	21/4	10	**Parotid (L)** Right Left **Submandibular (L)** Right Left	2.57 ± 0.48 2.80 ± 0.44 2.20 ± 0.28 2.39 ± 0.39	1.78 ± 0.15 1.79 ± 0.13 1.80 ± 0.14 1.81 ± 0.14	–	–
Xu *et al.*, 2023; China	Cross-sectional	47	27	53.0	25/2	20	53.9	20/0	3	**Parotid (L)** **Submandibular (L)**	1.84 ± 0.22 1.93 ± 0.19	1.59 ± 0.12 1.77 ± 0.10	10.65 ± 2.76 11.48 ± 2.21	7.77 ± 1.16 9.59 ± 1.03

Note: F, female; kPa, kilopascal; L, longitudinal; M, male; m/s, meters per second; *n*, number of individuals; NI, not informed; T, transverse. Data of shear wave elastography are presented as mean ± standard deviation.

Table 2. Clinical data from 530 patients with Sjögren's disease enrolled in the 11 retrieved studies

Study/SD patients	Disease duration (months)	ESSPRI or ESSDAI disease activity index (mean ± SD or median (range)	EULAR 2016						Additional tests (types)		
			Focus score ≥ 1, *n* (%)	Xerostomia (present), *n* (%)	Salivary flow	Xerophthalmia (present), *n* (%)	Schirmer (positive), *n* (%)	Anti-SSA-Ro (positive), *n* (%)	Anti-SSB-La (positive), *n* (%)	RF (positive), *n* (%)	ANA (positive), *n* (%)
Arslan *et al.*, 2020; *n*=53	47.6 ± 27.9	NI	24 (45.2)	48 (90.6)	NI	49 (92.4)	47 (88.6)	23 (43.3)	12 (22.6)	18 (33.9)	43 (81.1)
Bădărînză *et al.*, 2020; *n*=35	34	NI	(65.7)	(94.3)	NI	(94.3)	NI	(80)	(42.9)	(71.4)	NI
Caraba *et al.*, 2019; *n*=32	45.6 ± 14.4	NI	NI	NI	1.17 ± 0.38 g/2 min[c]	NI	32 (100)	32 (100)	32 (100)	32 (100)	32 (100)
Güngör *et al.*, 2022; *n*=47	31.8 ± 33	NI	NI	86 (100)	NI	86 (100)	86 (100)	NI	NI	NI	NI
Karadeniz *et al.*, 2023; *n*=46	≤48; 48-96; >96	5 [1-9.3][a]	31 (79.5)	28 (60.9)	NI	30 (65.2)	15 (37.5)	25 (58.1)	32 (76.2)	16 (45.7)	28 (60.9)
Ozer *et al.*, 2023; *n*=74	50.8 ± 28.4	6.26 ± 2.50[b]	31 (41.9)	72 (97.3)	NI	73 (98.6)	46 (62.2)	53 (71.6)	44 (59.5)	19 (25.7)	50 (67.6)
Prata *et al.*, 2022; *n*=50	148 ± 84	NI	NI	48 (96.0)	NI	50 (100)	42 (84.0)	47 (94.0)	26 (52.0)	NI	NI

Satis *et al.*, 2020; *n*=96	60	NI	NI	95 (100)	NI	95 (100)	NI	95 (100)	NI	NI	95 (100)
Swiecka *et al.*, 2022; *n*=45	NI	NI	NI	30 (68.2)	NI	NI	NI	NI	NI	NI	NI
Turnaoglu *et al.*, 2018; *n*=25	44.5	NI	NI	22 (88)	NI	24 (96)	22 (88.0)	9 (36.0)	4 (16.0)	6 (24.0)	21 (84.0)
Xu *et al.*, 2023; *n*=27	72.0 ± 56.4	NI	NI	NI	NI	NI	NI	27 (100)	NI	NI	NI

Note: ANA, anti-nuclear antibodies; NI, not informed; RF, rheumatoid factor; SSA, Sjögren's syndrome-related antigen A autoantibodies; SSB, Sjögren's syndrome-related antigen B autoantibodies.
[a]EULAR Sjogren’s Syndrome Patient-Reported Index (ESSPRI).
[b]EULAR Sjogren’s Syndrome Disease Activity Index (ESSDAI).
[c]Saxon test applied to measure the amount of stimulated saliva.
The results are expressed as mean ± standard deviation (SD), percent (%), or median (interquartile range).

Supplementary Files

Shear wave elastography of salivary glands in Sjögren disease: a novel protocol and meta-analysis

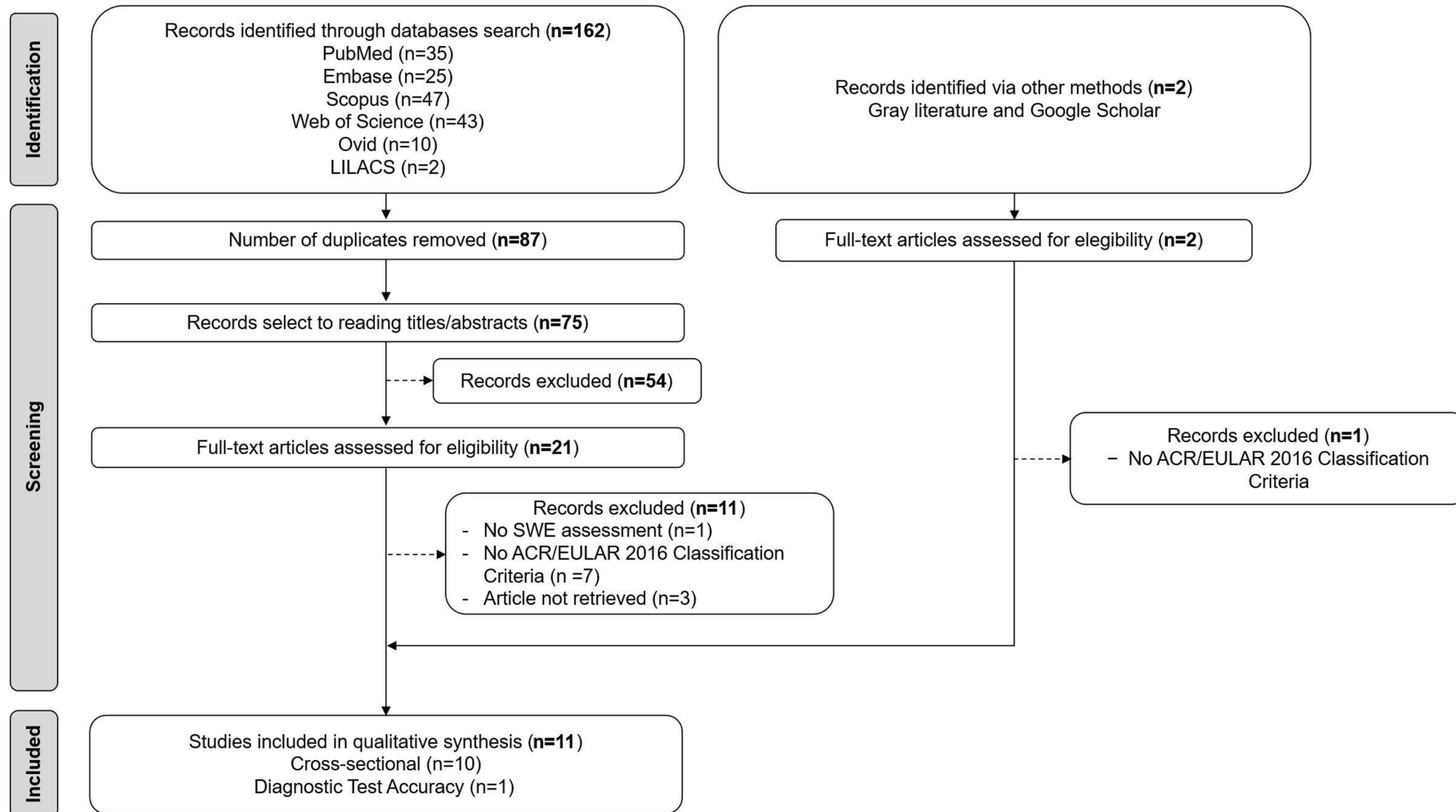
Table of contents

Supplementary File 1. Search strategies employed to identify articles in electronic databases

PubMed, Web of Science, and LILACS	elastography OR shear-wave OR shear wave OR S-wave OR shear-wave elastography OR shear wave elastography OR sonoelastography OR shear wave sonoelastography OR shear-wave sonoelastography OR elastometry OR elastographic OR sonoelastographic AND Sjogren syndrome OR Sjögren syndrome OR Sjögren’s syndrome OR Sjogren’s syndrome OR Sjögren disease OR sicca syndrome AND major salivary gland OR parotid gland OR submandibular gland OR sublingual gland
Scopus	elastography OR shear-wave OR “shear wave” OR S-wave OR “shear-wave elastography” OR “shear wave elastography” OR sonoelastography OR “shear wave sonoelastography” OR “shear-wave sonoelastography” OR elastometry OR elastographic OR sonoelastographic AND “Sjogren syndrome” OR “Sjögren syndrome” OR “Sjögren’s syndrome” OR “Sjogren’s syndrome” OR “Sjögren disease” OR “sicca syndrome” AND “major salivary gland” OR “parotid gland” OR “submandibular gland” OR “sublingual gland”

Embase	elastography OR shear-wave OR “shear wave” OR S-wave OR “shear-wave elastography” OR “shear wave elastography” OR sonoelastography OR “shear wave sonoelastography” OR “shear-wave sonoelastography” OR elastometry OR elastographic OR sonoelastographic AND “Sjogren syndrome” OR “Sjögren syndrome” OR “Sjögren disease” OR “sicca syndrome” AND “major salivary gland” OR “parotid gland” OR “submandibular gland” OR “sublingual gland”
Ovid	elastography OR shear-wave OR shear wave OR S-wave OR shear-wave elastography OR shear wave elastography OR sonoelastography OR shear wave sonoelastography OR shear-wave sonoelastography OR elastometry OR elastographic OR sonoelastographic AND Sjogren syndrome OR Sjogren disease OR sicca syndrome AND major salivary gland OR parotid gland OR submandibular gland OR sublingual gland

Supplementary File 2. Flowchart depicting article selection process



Supplementary File 3. Results of studies investigating the association between shear wave elastography of the salivary glands and clinical parameters

Study	Age	Disease duration	ESSPRI or ESSDAI index	Xerostomia	Salivary flow	Xerophthalmia	Schirmer	Parotid gland enlargement	Arthralgia/arthritis	Focus score	Anti-SSA/Ro	Anti SSB/La	ANA	RF	Beta-2 serum microglobulin	Gama globulin	Laboratory concentrations (C3, C4, ESR)
Bădărînză *et al.*, 2020	–	–	–	–	–	–	–	Yes	–	–	No	No	–	Yes	–	–	Yes (C4 levels)
Caraba *et al.*, 2019	–	–	–	–	Yes (-)	–	–	–	–	Yes	–	–	–	–	Yes	–	–
Güngör *et al.*, 2022	–	No	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Karadeniz *et al.*, 2023	No	No	No (ESSPRI)	No	–	No	Yes (-)	–	No	No	No	No	No	No	–	–	No (C3, C4 levels)
Özer *et al.*, 2023	No	No	No (ESSDAI)	–	–	–	No	–	–	No	No	No	No	No	–	–	No (ESR)
Świecka *et al.*, 2022	–	–	–	–	–	–	–	–	–	–	–	–	Yes	Yes	–	Yes	No (C3, C4, ESR)
Turnaoglu *et al.*, 2018	–	No	–	No	–	–	–	–	–	–	–	–	–	–	–	–	–

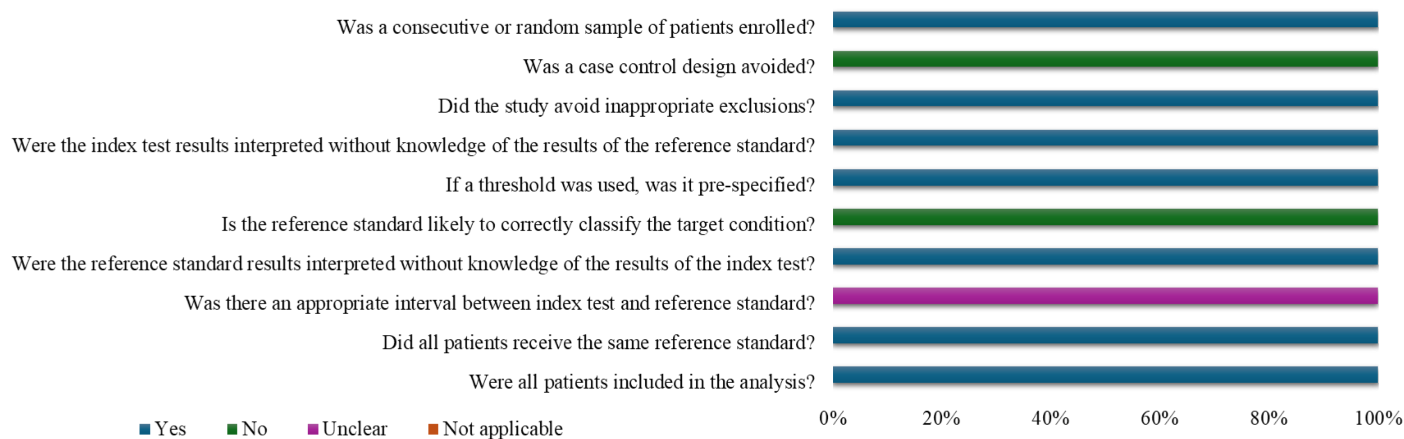
Note: Yes, presence of association or correlation; No, absence of association or correlation; ESR, Erytrocite sedimentation rate.

Supplementary File 4. Technical aspects of shear wave elastography

Study	Evaluated major salivary glands	Number of regions evaluated	Measures
Arslan *et al.*, 2020	Parotid and submandibular glands (bilateral)	1 (NI)	1
Bădărînză *et al.*, 2020	Parotid and submandibular glands (bilateral)	1 (NI)	3
Caraba *et al.*, 2019	Parotid and submandibular glands (bilateral)	3: central, peripheral, and subcapsular	6
Güngör *et al.*, 2022	Parotid and submandibular glands (bilateral)	1: same region for both methods	E1: 4; E2:1
Karadeniz *et al.*, 2023	Parotid grands (bilateral)	1 (NI)	3
Özer *et al.*, 2023	Parotid and submandibular glands (bilateral)	≥2 (NI)	3
Prata *et al.*, 2022	Parotid and submandibular glands (bilateral)	6: 3 peripheral and 3 central	6
Satış *et al.*, 2020	Parotid and submandibular glands (bilateral)	1: mid-gland	3
Świecka *et al.*, 2022	Parotid and submandibular glands (bilateral)	1 (NI)	5
Turnaoglu *et al.*, 2018	Parotid and submandibular glands (bilateral)	1: parotid - center of the caudal pole; submandibular - center of the gland	10
Xu *et al.*, 2023	Parotid and submandibular glands (bilateral)	1 (NI)	3

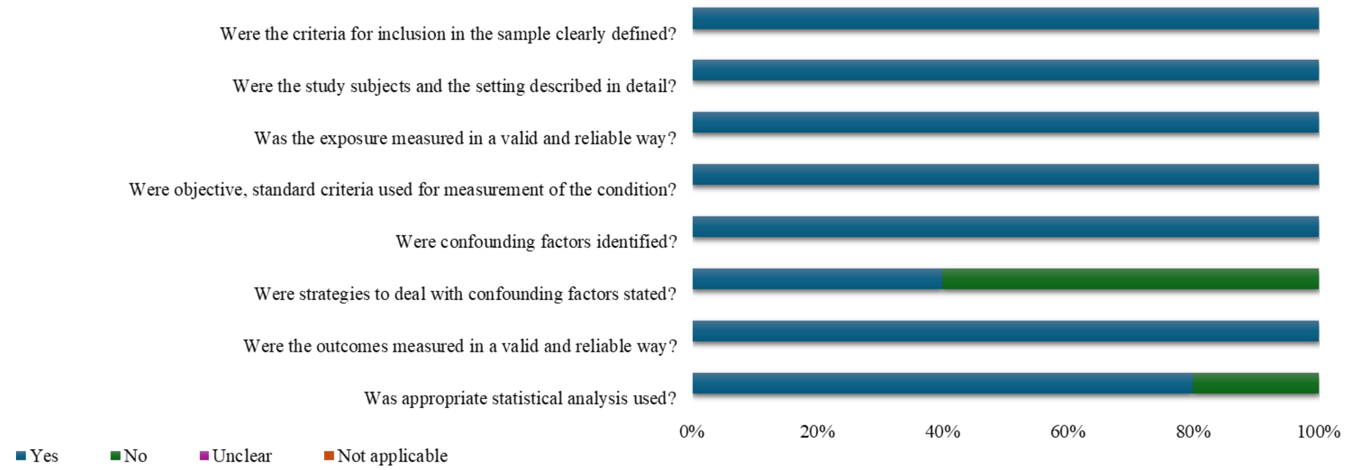
Supplementary File 5. Joanna Briggs Institute critical appraisal checklist for accuracy studies

Study	Items									
	Was a consecutive or random sample of patients enrolled?	*Was a case control design avoided?*	*Did the study avoid inappropriate exclusions?*	*Were the index test results interpreted without knowledge of the results of the reference standard?*	*If a threshold was used, was it pre-specified?*	*Is the reference standard likely to correctly classify the target condition?*	*Were the reference standard results interpreted without knowledge of the results of the index test?*	*Was there an appropriate interval between index test and reference standard?*	*Did all patients receive the same reference standard*	*Were all patients included in the analysis?*
Güngör *et al.*, 2022	Yes	No	Yes	Yes	Yes	No	Yes	Unclear	Yes	Yes



Supplementary File 6. Joanna Briggs Institute critical appraisal checklist for cross-sectional studies

Study	Items							
	Were the criteria for inclusion in the sample clearly defined?	*Were the study subjects and the setting described in detail??*	*Was the exposure measured in a valid and reliable way?*	*Were objective, standard criteria used for measurement of the condition?*	*Were confounding factors identified?*	*Were strategies to deal with confounding factors stated?*	*Were the outcomes measured in a valid and reliable way?*	*Was appropriate statistical analysis used?*
Arslan *et al.*, (2020)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Bădărînză *et al.*, (2020)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Caraba *et al.*, (2019)	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Karadeniz *et al.*, (2023)	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Özer *et al.*, (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prata *et al.*, (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Satış *et al.*, (2020)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Świecka *et al.*, (2022)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Turnaoglu *et al.*, (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Xu *et al.*, (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes



Were the criteria for inclusion in the sample clearly defined?
Were the study subjects and the setting described in detail?
Was the exposure measured in a valid and reliable way?
Were objective, standard criteria used for measurement of the condition?
Were confounding factors identified?
Were strategies to deal with confounding factors stated?
Were the outcomes measured in a valid and reliable way?
Was appropriate statistical analysis used?
0%
20%
40%
60%
80%
100%
Yes
No
Unclear
Not applicable

References

1. Alfuraih AM, O'Connor P, Hensor E, Tan AL, Emery P, Wakefield RJ. The effect of unit, depth, and probe load on the reliability of muscle shear wave elastography: variables affecting reliability of SWE. J Clin Ultrasound. 2018;46(2):108-15. doi:10.1002/jcu.22534.
2. Arslan S, Durmaz MS, Erdogan H, Esmen SE, Turgut B, Iyisoy MS. Two-dimensional shear wave elastography in the assessment of salivary gland involvement in primary Sjögren's syndrome. J Ultrasound Med. 2020;39(5):949-56. doi:10.1002/jum.15179.
3. Bădărînză M, Serban O, Maghear L, Bocsa C, Micu M, Damian L, et al. Shear wave elastography as a new method to identify parotid lymphoma in primary Sjögren Syndrome patients: an observational study. Rheumatol Int. 2020;40(8):1275-1281. doi: 10.1007/s00296-020-04548-x.
4. Baer AN, Hammitt KM. Sjögren's disease, not syndrome. Arthritis Rheumatol. 2021;73(7):1347-1348. doi: 10.1002/art.41676.
5. Baldini C, Fulvio G, La Rocca G, Ferro F. Update on the pathophysiology and treatment of primary Sjögren syndrome. Nat Rev Rheumatol. 2024;20(8):473-491. doi: 10.1038/s41584-024-01135-3.
6. Beydon M, McCoy S, Nguyen Y, Sumida T, Mariette X, Seror R. Epidemiology of Sjögren syndrome. Nat Rev Rheumatol. 2024;20(3):158-169. doi: 10.1038/s41584-023-01057-6.
7. Campbell JM, Klugar M, Ding S, Carmody DP, Hakonsen SJ, Jadotte YT, et al. Diagnostic test accuracy: methods for systematic review and meta-analysis. Int J Evid Based Healthc. 2015;13(3):154-62. doi: 10.1097/XEB.0000000000000061.

8. Caraba A, Babalic FC, Iurciuc S, Iurciuc M. The utility of major salivary gland ultrasonographic parameters in the diagnosis of Sjögren syndrome. Dis Markers. 2019;1716848. doi:10.1155/2019/1716848.
9. Carotti M, Ciapetti A, Jousse-Joulin S, Salaffi F. Ultrasonography of the salivary glands: the role of grey-scale and colour/power Doppler. Clin Exp Rheumatol. 2014 Jan-Feb;32(1 Suppl 80):S61-70.
10. Chen S, Wang Y, Chen S, Wu Q, Chen S. Virtual touch quantification of the salivary glands for diagnosis of primary Sjögren syndrome. J Ultrasound Med. 2016;35(12):2607-13. doi:10.7863/ultra.16.01085.
11. Chen YF, Hsieh AH, Fang YF, Kuo CF. Diagnostic evaluation using salivary gland ultrasonography in primary Sjögren's syndrome. J Clin Med. 2023;12(6):2428. doi:10.3390/jcm12062428.
12. Cindil E, Oktar SO, Akkan K, Sendur HN, Mercan R, Tufan A, Ozturk MA. Ultrasound elastography in assessment of salivary glands involvement in primary Sjögren's syndrome. Clin Imaging. 2018;50:229-34. doi: 10.1016/j.clinimag.2018.04.011.
13. Cosgrove D, Piscaglia F, Bamber J, Bojunga J, Correas JM, Gilja OH, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: clinical applications. Ultraschall Med. 2013;34(3):238-53. doi: 10.1055/s-0033-1335375.
14. Dai X, Sui X, Chen S, Zhao B, Liu Z, Wang X. The diagnostic performance of salivary gland ultrasound elastography in Sjögren's syndrome and sicca symptoms: a systematic review and meta-analysis. Eur Radiol. 2024;34(3):1545-1555. doi: 10.1007/s00330-023-10166-5.

15. de Moraes FP, Florezi GP, Hsieh R, Dos Santos CP, Andriolo F, Lourenço SV. A morphological post mortem profile in minor salivary glands changes in females. J Mol Histol. 2024 Dec 6;56(1):32. doi: 10.1007/s10735-024-10306-1.
16. de Oliveira FR, Appenzeller S, Pasoto SG, Fernandes MLMS, Lemos Lopes ML, de Magalhães Souza Fialho SC, et al. Recommendations on neurologic, cognitive, and psychiatric manifestations in patients with Sjögren's disease by the Brazilian Society of Rheumatology. Adv Rheumatol. 2025;65(1):7. doi: 10.1186/s42358-025-00438-7.
17. de Oliveira FR, Motta ACF, Módulo CM, Garcia DM, Chiorini JA, Louzada-Junior P, et al. Clinical and laboratory evaluation of sicca complaints: distinctive aspects of primary, secondary and non-Sjogren syndrome. Adv Rheumatol. 2022;62(1):23. doi: 10.1186/s42358-022-00255-2.
18. Filho RHC, Pereira FL, Iared W. Diagnostic accuracy evaluation of two-dimensional shear wave elastography in the differentiation between benign and malignant thyroid nodules: systematic review and meta-analysis. J Ultrasound Med. 2020;39(9):1729-1741. doi: 10.1002/jum.15271.
19. Finzel S, Jousse-Joulin S, Costantino F, Hánová P, Hocevar A, Iagnocco A, et al. Patient-based reliability of the Outcome Measures in Rheumatology (OMERACT) ultrasound scoring system for salivary gland assessment in patients with Sjögren's syndrome. Rheumatology (Oxford). 2021;60(5):2169-76. doi:10.1093/rheumatology/keaa471.
20. Fisher BA, Everett CC, Rout J, O'Dwyer JL, Emery P, Pitzalis C, et al. Effect of rituximab on a salivary gland ultrasound score in primary Sjogren’s syndrome: results of the TRACTISS randomised double-blind multicentre substudy. Ann. Rheum. Dis. 2018;77(3)412-16. doi:10.1136/annrheumdis-2017-212268.

21. Güngör Ö, Şahin K, Öztürk C, Uysal Ramadan S, Can S, Kaşıkcı M. Ultrasound elastography findings in Sjögren's syndrome. Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi. 2022;55(1):23-27. doi:10.20492/aeahtd.982022.
22. Haddaway NR, Collins AM, Coughlin D, Kirk S. The role of Google Scholar in evidence reviews and its applicability to grey literature searching. PLoS One. 2015;10(9):e0138237. doi: 10.1371/journal.pone.0138237.
23. Hocevar A, Ambrozic A, Rozman B, Kveder T, Tomsic M. Ultrasonographic changes of major salivary glands in primary Sjogren's syndrome. Diagnostic value of a novel scoring system. Rheumatology (Oxford). 2005;44(6):768-72. doi:10.1093/rheumatology/keh588.
24. Hofauer B, Mansour N, Heiser C, Gahleitner C, Thuermel K, Bas M, Knopf A. Sonoelastographic modalities in the evaluation of salivary gland characteristics in Sjögren's syndrome. Ultrasound Med Biol. 2016;42(9):2130-9. doi: 10.1016/j.ultrasmedbio.2016.04.011.
25. Inanc N, Şahinkaya Y, Mumcu G, Türe Özdemir F, Paksoy A, Ertürk Z, Direskeneli H, Bruyn GA. Evaluation of salivary gland ultrasonography in primary Sjögren's syndrome: does it reflect clinical activity and outcome of the disease? Clin Exp Rheumatol. 2019;37 Suppl 118(3):140-45.
26. Jousse-Joulin S, Coiffier G. Current status of imaging of Sjogren's syndrome. Best Pract Res Clin Rheumatol. 2020;34(6):101592. doi:10.1016/j.berh.2020.101592.
27. Jousse-Joulin S, Devauchelle-Pensec V, Cornec D, Marhadour T, Bressollette L, Gestin S, Pers JO, Nowak E, Saraux A. Brief report: ultrasonographic assessment of salivary gland response to rituximab in primary Sjögren's syndrome. Arthritis Rheumatol. 2015 Jun;67(6):1623-8. doi: 10.1002/art.39088.

28. Jousse-Joulin S, Milic V, Jonsson MV, Plagou A, Theander E, Luciano N, et al. Is salivary gland ultrasonography a useful tool in Sjögren's syndrome? A systematic review. Rheumatology (Oxford). 2016;55(5):789-800. doi: 10.1093/rheumatology/kev385.
29. Karadeniz H, Cerit M, Güler AA, Salman RB, Satış H, Yıldırım D, et al. Lacrimal gland ultrasonography and elastography as a diagnostic and activity tool for primary Sjögren's syndrome. Int J Rheum Dis. 2023;26(6):1083-90. doi:10.1111/1756-185X.14702.
30. Lee KA, Lee SH, Kim HR. Ultrasonographic changes of major salivary glands in primary Sjögren's syndrome. J Clin Med. 2020;9(3):803. doi:10.3390/jcm9030803.
31. Leong SS, Jalalonmuhali M, Md Shah MN, Ng KH, Vijayananthan A, Hisham R, et al. Ultrasound shear wave elastography for the evaluation of renal pathological changes in adult patients. Br J Radiol. 2023;96(1144):20220288. doi: 10.1259/bjr.20220288.
32. Liu J, Xia G, Dai Z, Wang R, Feng Z, Ma G, et al. Accuracy of two-dimensional transverse wave elastography of salivary glands in diagnosis of Sjögren's disease: a systematic review and meta-analysis. BMJ Open. 2024;14(8):e081015. doi: 10.1136/bmjopen-2023-081015.
33. Ma D, Feng Y, Lin X. Immune and non-immune mediators in the fibrosis pathogenesis of salivary gland in Sjögren's syndrome. Front Immunol. 2024 Oct 14;15:1421436. doi: 10.3389/fimmu.2024.1421436.
34. Makula E, Pokorny G, Rajtár M, Kiss I, Kovács A, Kovács L. Parotid gland ultrasonography as a diagnostic tool in primary Sjögren's syndrome. Br J Rheumatol. 1996;35(10):972-77. doi:10.1093/rheumatology/35.10.972.

35. Manfrè V, Giovannini I, Zandonella Callegher S, Lorenzon M, Pegolo E, Tel A, et al. Ultrasound and bioptic investigation of patients with primary Sjögren's syndrome. J Clin Med. 2021;10(6):1171. doi: 10.3390/jcm10061171.
36. Mariette X, Criswell LA. Primary Sjögren's Syndrome. N Engl J Med. 2018;378(10):931-939. doi: 10.1056/NEJMcp1702514.
37. Martins FB, Oliveira MB, Oliveira LM, Lourenço AG, Paranhos LR, Motta ACF. Diagnostic accuracy of ultrasonography in relation to salivary gland biopsy in Sjögren's syndrome: a systematic review with meta-analysis. Dentomaxillofac Radiol. 2024;53(2):91-102. doi: 10.1093/dmfr/twad007.
38. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis. JBI, 2020. Available from https://synthesismanual.jbi.global.
39. Mossel E, Delli K, van Nimwegen JF, Stel AJ, Kroese FGM, Spijkervet FKL, et al. Ultrasonography of major salivary glands compared with parotid and labial gland biopsy and classification criteria in patients with clinically suspected primary Sjögren's syndrome. Ann Rheum Dis. 2017;76(11):1883-89. doi: 10.1136/annrheumdis-2017-211250.
40. Oruk YE, Çildağ MB, Karaman CZ, Çildağ S. Effectiveness of ultrasonography and shear wave sonoelastography in Sjögren syndrome with salivary gland involvement. Ultrasonography. 2021;40(4):584-593. doi: 10.14366/usg.21014.
41. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4.

42. Oxholm P. Primary Sjögren's syndrome--clinical and laboratory markers of disease activity. Semin Arthritis Rheum. 1992;22(2):114-26. doi:10.1016/0049-0172(92)90005-x.
43. Özer H, Tezcan D, Hakbilen S, Gülcemal S, Topaloğlu ÖF, Yazol M, Yılmaz S. Diagnostic performance of gray-scale ultrasound and shear wave elastography in assessing salivary gland involvement in patients with primary Sjögren's syndrome. J Clin Ultrasound. 2023;51(1):187-94. doi:10.1002/jcu.23379.
44. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71.
45. Park SY, Kang BJ. Combination of shear-wave elastography with ultrasonography for detection of breast cancer and reduction of unnecessary biopsies: a systematic review and meta-analysis. Ultrasonography. 2021;40(3):318-332. doi: 10.14366/usg.20058.
46. Prata AR, Freitas JP, Marques ML, Costa F, Santiago M, Serra S, et al. Shear-wave elastography evaluation of major salivary glands in primary Sjögren’s syndrome. ARP Rheumatol. 2022;1(3):197-204.
47. Price EJ, Benjamin S, Bombardieri M, Bowman S, Carty S, Ciurtin C, et al. British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease. Rheumatology (Oxford). 2025;64(2):409-439. doi: 10.1093/rheumatology/keae152.
48. Proctor GB, Shaalan AM. Disease-induced changes in salivary gland function and the composition of saliva. J Dent Res. 2021;100(11):1201-09. doi:10.1177/00220345211004842.

49. Rebel D, de Wolff L, Delli K, Stel AJ, Kokol HC, Vissink A, et al. Added value of the salivary gland ultrasonography OMERACT score in the ACR/EULAR classification criteria for Sjögren's disease. Semin Arthritis Rheum. 2024;67:152473. doi:10.1016/j.semarthrit.2024.152473.
50. Satış H, Cindil E, Salman RB, Yapar D, Demir NB, Temel E, et al. Parotid elastography: a potential alternative to replace labial biopsy in classification of patients with primary Sjögren's syndrome? Clin Rheumatol. 2020;39(12):3707-13. doi:10.1007/s10067-020-05146-9.
51. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, et al. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for primary sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. Arthritis Rheumatol. 2017;69(1):35-45. doi: 10.1002/art.39859.
52. Świecka M, Paluch Ł, Pietruski P, Maślińska M, Zakrzewski J, Kwiatkowska B. Shear wave elastography as a potential additional diagnostic tool in primary Sjögren's syndrome: an observational study. Rheumatol Int. 2022;42(9):1579-87. doi:10.1007/s00296-022-05120-5.
53. Trevisani VFM, Pasoto SG, Fernandes MLMS, Lopes MLL, de Magalhães Souza Fialho SC, Pinheiro AC, et al. Recommendations from the Brazilian society of rheumatology for the diagnosis of Sjögren's syndrome (Part I): glandular manifestations (systematic review). Adv Rheumatol. 2019;59(1):58. doi: 10.1186/s42358-019-0102-8.
54. Trevisani VFM, Pinheiro AC, de Magalhães Souza Fialho SC, Fernandes MLMS, Pugliesi A, Pasoto SG, et al. Recommendations for evaluation and diagnosis of extra-glandular manifestations of primary Sjögren syndrome:

results of an epidemiologic systematic review/meta-analysis and a consensus guideline from the Brazilian society of rheumatology (hepatic, gastrointestinal and pancreatic). Adv Rheumatol. 2022;62(1):35. doi: 10.1186/s42358-022-00267-y.

55. Trevisani VFM, Pugliesi A, Pasoto SG, Lopes MLL, Guedes LKN, Miyamoto ST, et al. Recommendations for evaluation and diagnosis of extra-glandular manifestations of primary sjogren syndrome: results of an epidemiologic systematic review/meta-analysis and a consensus guideline from the Brazilian Society of Rheumatology (articular, pulmonary and renal). Adv Rheumatol. 2022;62(1):18. doi: 10.1186/s42358-022-00248-1.
56. Turnaoglu H, Kural Rahatli F, Pamukcu M, Haberal KM, Uslu N. Diagnostic value of acoustic radiation force impulse imaging in the assessment of salivary gland involvement in primary Sjögren's syndrome. Med Ultrason. 2018;20(3):313-18. doi:10.11152/mu-1397.
57. van Nimwegen JF, Mossel E, Delli K, van Ginkel MS, Stel AJ, Kroese FGM, et al. Incorporation of salivary gland ultrasonography into the American College of Rheumatology/European League Against Rheumatism Criteria for primary sjögren's syndrome. Arthritis Care Res (Hoboken). 2020;72(4):583-590. doi: 10.1002/acr.24017.
58. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014 19;14:135. doi:10.1186/1471-2288-14-135.
59. Wierzbicka M, Kałużny J, Ruchała M, Stajgis M, Kopeć T, Szyfter W. Sonoelastography--a useful adjunct for parotid gland ultrasound assessment in

patients suffering from chronic inflammation. Med Sci Monit. 2014;20:2311-7. doi:10.12659/MSM.890678.

60. Wise CM, Agudelo CA, Semble EL, Stump TE, Woodruff RD. Comparison of parotid and minor salivary gland biopsy specimens in the diagnosis of Sjögren's syndrome. Arthritis Rheum. 1988;31(5):662-6. doi:10.1002/art.1780310512.

61. Xu Z, Li R, Xia B, Jiang M, Wu X, Zhang X, et al. Combination of ultra-micro angiography and sound touch elastography for diagnosis of primary Sjögren's syndrome: a diagnostic test. Quant Imaging Med Surg. 2023;13(10):7170-79. doi:10.21037/qims-23-711.

62. Zandonella Callegher S, Giovannini I, Zenz S, Manfrè V, Stradner MH, Hocevar A, et al. Sjögren syndrome: looking forward to the future. Ther Adv Musculoskelet Dis. 2022 May 23;14:1759720X221100295. doi: 10.1177/1759720X221100295.

63. Zhan Q, Zhang J, Lin Y, Chen W, Fan X, Zhang D. Pathogenesis and treatment of Sjogren's syndrome: Review and update. Front Immunol. 2023;14:1127417. doi: 10.3389/fimmu.2023.1127417.

64. Zhang M, Pan J, Sheng J. Systematic review and meta-analysis of the diagnostic performance of lacrimal gland ultrasound elastography in primary Sjögren's syndrome. Int Ophthalmol. 2024;44(1):271. doi: 10.1007/s10792-024-03185-8.

5 CONSIDERAÇÕES FINAIS

Este estudo teve como objetivos propor um protocolo reprodutível para a aplicação da SWE na triagem da DS e revisar sistematicamente seu desempenho diagnóstico nas principais glândulas salivares, conforme os critérios ACR/EULAR de 2016. Os resultados da revisão sistemática demonstraram que a SWE é eficaz na diferenciação entre pacientes com DS e controles saudáveis, especialmente quando aplicada à glândula parótida e interpretada em kPa. Os dados sugerem que a SWE agrega valor diagnóstico além da US, destacando-se como uma ferramenta não invasiva e promissora para a avaliação da doença. Por um outro lado, na série de casos realizada, seguindo um novo protocolo de realização do exame e aquisição dos valores de SWE, apesar de poucos casos incluídos, os valores de SWE, expressos em kPa e m/s, variaram entre os grupos do estudo e entre regiões de uma mesma glândula. Observamos valores heterogêneos de rigidez em diferentes regiões do parênquima, tanto nas glândulas parótidas quanto nas submandibulares, bilateralmente, apontando que a análise em única região da glândula, pode não ser representativa das alterações como um todo. Com base nisso, limitar a SWE a uma única glândula, região ou plano de imagem pode ocultar alterações relacionadas à doença, especialmente em casos de envolvimento inicial ou focal. Futuros estudos devem priorizar protocolos padronizados com a necessidade de consenso sobre parâmetros técnicos e incluir grupos de amostras com síndrome sicca não relacionada à DS, a fim de consolidar a contribuição dessa técnica para o diagnóstico.

REFERÊNCIAS

ALFURAIH, A. M. *et al*. The effect of unit, depth, and probe load on the reliability of muscle shear wave elastography: variables affecting reliability of SWE. **Journal of Clinical Ultrasound**, v. 46, n. 2, p. 108-115, 2018. DOI: 10.1002/jcu.22534.

ALMANNAI, A. I. *et al*. Accuracy of Labial Salivary Gland Biopsy in Suspected Cases of Sjogren's Syndrome. **Cureus**, v. 16, n. 11, e74746, 2024. DOI: 10.7759/cureus.74746

ARSLAN, S. *et al*. Two-dimensional shear wave elastography in the assessment of salivary gland involvement in primary Sjögren's syndrome. **Journal of Ultrasound in Medicine**, v. 39, n. 5, p. 949-956, 2020. DOI: 10.1002/jum.15179.

BĂDĂRÎNZĂ, M. *et al*. Shear wave elastography as a new method to identify parotid lymphoma in primary Sjögren Syndrome patients: an observational study**. Rheumatology Internationa**l, v. 40, n. 8, p. 1275-1281, 2020. DOI: 10.1007/s00296-020-04548-x.

BAER, A. N.; HAMMITT, K. M. Sjögren's disease, not syndrome. **Arthritis & Rheumatology**, v. 73, n. 7, p. 1347-1348, 2021. DOI: 10.1002/art.41676.

BALDINI, C. *et al***.** Update on the pathophysiology and treatment of primary Sjögren syndrome. **Nature Reviews Rheumatology**, v. 20, n. 8, p. 473-491, 2024. DOI: 10.1038/s41584-024-01135-3.

BEYDON, M. *et al***.** Epidemiology of Sjögren syndrome. **Nature Reviews Rheumatology**, v. 20, n. 3, p. 158-169, 2024. DOI: 10.1038/s41584-023-01057-6.

CAMPBELL, J. M. *et al*. Diagnostic test accuracy: methods for systematic review and meta-analysis. **International Journal of Evidence-Based Healthcare**, v. 13, n. 3, p. 154-162, 2015. DOI: 10.1097/XEB.0000000000000061.

CARABA, A. *et al*. The utility of major salivary gland ultrasonographic parameters in the diagnosis of Sjögren syndrome. **Disease Markers**, v. 2019, 2019. DOI: 10.1155/2019/1716848.

CARNEIRO FILHO, R. H.; PEREIRA, F. L.; IARED, W. Diagnostic accuracy evaluation of two-dimensional shear wave elastography in the differentiation between benign and malignant thyroid nodules: systematic review and meta-analysis. **Journal of Ultrasound in Medicine**, v. 39, n. 9, p. 1729-1741, 2020. DOI: 10.1002/jum.15271.

CAROTTI, M. *et al*. Ultrasonography of the salivary glands: the role of grey-scale and colour/power Doppler. **Clinical and Experimental Rheumatology**, v. 32, n. 1, p. S61-S70, 2014.

CHEN, S. *et al*. Virtual touch quantification of the salivary glands for diagnosis of primary Sjögren syndrome. **Journal of Ultrasound in Medicine**, v. 35, n. 12, p. 2607-2613, 2016. DOI: 10.7863/ultra.16.01085.

CHEN, Y. F. *et al*. Diagnostic evaluation using salivary gland ultrasonography in primary Sjögren's syndrome. **Journal of Clinical Medicine**, v. 12, n. 6, p. 2428, 2023. DOI: 10.3390/jcm12062428.

CINDIL, E. *et al*. Ultrasound elastography in assessment of salivary glands involvement in primary Sjögren's syndrome. **Clinical Imaging**, v. 50, p. 229-234, 2018. DOI: 10.1016/j.clinimag.2018.04.011.

COSGROVE, D. *et al.* EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: clinical applications. **Ultraschall in der Medizin**, v. 34, n. 3, p. 238-253, 2013. DOI: 10.1055/s-0033-1335375.

DAI, X. *et al.* The diagnostic performance of salivary gland ultrasound elastography in Sjögren's syndrome and sicca symptoms: a systematic review and meta-analysis. **European Radiology**, v. 34, n. 3, p. 1545-1555, 2024. DOI: 10.1007/s00330-023-10166-5.

DIAS, L. H. *et al.* Pain and fatigue are predictors of quality of life in primary Sjögren's syndrome. **Advances in Rheumatology**, v. 61, n. 1, 28, 2021. DOI: 10.1186/s42358-021-00181-9.

FANA, V.; TERSLEV, L. Lacrimal and salivary gland ultrasound - how and when to use in patients with primary Sjögren's syndrome. **Best practice & research. Clinical Rheumatology**, v. 37, n. 1, e:101837, 2024. DOI: 10.1016/j.berh.2023.101837

FANA, V. *et al*. Application of the OMERACT Grey-scale Ultrasound Scoring System for salivary glands in a single-centre cohort of patients with suspected Sjögren's syndrome. **RMD Open**, v. 7, n. 2, e:001516, 2021. DOI: 10.1136/rmdopen-2020-001516.

FINZEL, S. *et al.* Patient-based reliability of the Outcome Measures in Rheumatology (OMERACT) ultrasound scoring system for salivary gland assessment in patients with Sjögren's syndrome. **Rheumatology**, v. 60, n. 5, p. 2169-2176, 2021. DOI: 10.1093/rheumatology/keaa471.

FISHER, B. A. *et al*. Standardisation of labial salivary gland histopathology in clinical trials in primary Sjögren's syndrome. **Annals of the Rheumatic Diseases**, v. 76, n. 7, p. 1161-1168, 2017. DOI:10.1136/annrheumdis-2016-210448

FISHER, B. A. *et al.* Effect of rituximab on a salivary gland ultrasound score in primary Sjogren's syndrome: results of the TRACTISS randomised double-blind multicentre substudy. **Annals of the Rheumatic Diseases**, v. 77, n. 3, p. 412-416, 2018. DOI: 10.1136/annrheumdis-2017-212268.

GÜNGÖR, Ö. *et al.* Ultrasound elastography findings in Sjögren's syndrome. **Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi**, v. 55, n. 1, p. 23-27, 2022. DOI: 10.20492/aeahtd.982022.

HADDAWAY, N. R. *et al.* The role of Google Scholar in evidence reviews and its applicability to grey literature searching. **PLoS One**, v. 10, n. 9, e0138237, 2015. DOI: 10.1371/journal.pone.0138237.

HOCEVAR, A. *et al.* Ultrasonographic changes of major salivary glands in primary Sjogren's syndrome. Diagnostic value of a novel scoring system. **Rheumatology**, v. 44, n. 6, p. 768-772, 2005. DOI: 10.1093/rheumatology/keh588.

HOFAUER, B. *et al.* Sonoelastographic modalities in the evaluation of salivary gland characteristics in Sjögren's syndrome. **Ultrasound in Medicine and Biology**, v. 42, n. 9, p. 2130-2139, 2016. DOI: 10.1016/j.ultrasmedbio.2016.04.011.

INANC, N. *et al.* Evaluation of salivary gland ultrasonography in primary Sjögren's syndrome: does it reflect clinical activity and outcome of the disease? **Clinical and Experimental Rheumatology**, v. 37, Suppl. 118(3), p. 140-145, 2019.

JOUSSE-JOULIN, S.; COIFFIER, G. Current status of imaging of Sjogren's syndrome. **Best Practice & Research Clinical Rheumatology**, v. 34, n. 6, 101592, 2020. DOI: 10.1016/j.berh.2020.101592.

JOUSSE-JOULIN, S. *et al.* Brief report: ultrasonographic assessment of salivary gland response to rituximab in primary Sjögren's syndrome. **Arthritis & Rheumatology**, v. 67, n. 6, p. 1623-1628, 2015. DOI: 10.1002/art.39088.

JOUSSE-JOULIN, S. *et al.* Is salivary gland ultrasonography a useful tool in Sjögren's syndrome? A systematic review. **Rheumatology**, v. 55, n. 5, p. 789-800, 2016. DOI: 10.1093/rheumatology/kev385.

JOUSSE-JOULIN, S. *et al.* Video clip assessment of a salivary gland ultrasound scoring system in Sjögren's syndrome using consensual definitions: an OMERACT ultrasound working group reliability exercise. **Annals of the Rheumatic Diseases**, v. 78, n. 7, p. 967-973, 2019. DOI: 10.1136/annrheumdis-2019-215024.

JOUSSE-JOULIN, S. *et al.* Weight of salivary gland ultrasonography compared to other items of the 2016 ACR/EULAR classification criteria for Primary Sjögren's syndrome. **Journal of Internal Medicine**, v. 287, n. 2, p. 180-188, 2020. DOI: 10.1111/joim.12992.

KARADENIZ, H. *et al.* Lacrimal gland ultrasonography and elastography as a diagnostic and activity tool for primary Sjögren's syndrome. **International Journal of Rheumatic Diseases**, v. 26, n. 6, p. 1083-1090, 2023. DOI: 10.1111/1756-185X.14702.

LEE, K. A.; LEE, S. H.; KIM, H. R. Ultrasonographic changes of major salivary glands in primary Sjögren's syndrome. **Journal of Clinical Medicine**, v. 9, n. 3, 803, 2020. DOI: 10.3390/jcm9030803.

LEONG, S. S. *et al.* Ultrasound shear wave elastography for the evaluation of renal pathological changes in adult patients. **British Journal of Radiology**, v. 96, n. 1144, 20220288, 2023. DOI: 10.1259/bjr.20220288.

LIU, J. *et al.* Accuracy of two-dimensional transverse wave elastography of salivary glands in diagnosis of Sjögren's disease: a systematic review and meta-analysis. **BMJ Open**, v. 14, n. 8, e081015, 2024. DOI: 10.1136/bmjopen-2023-081015.

MA, D.; FENG, Y.; LIN, X. Immune and non-immune mediators in the fibrosis pathogenesis of salivary gland in Sjögren's syndrome. **Frontiers in Immunology**, v. 15, 1421436, 2024. DOI: 10.3389/fimmu.2024.1421436.

MAKULA, E. *et al.* Parotid gland ultrasonography as a diagnostic tool in primary Sjögren's syndrome. **British Journal of Rheumatology**, v. 35, n. 10, p. 972-977, 1996. DOI: 10.1093/rheumatology/35.10.972.

MANFRÈ, V. *et al.* Ultrasound and bioptic investigation of patients with primary Sjögren's syndrome. **Journal of Clinical Medicine**, v. 10, n. 6, 1171, 2021. DOI: 10.3390/jcm10061171.

MARIETTE, X.; CRISWELL, L. A. Primary Sjögren's Syndrome. **New England Journal of Medicine**, v. 378, n. 10, p. 931-939, 2018. DOI: 10.1056/NEJMcp1702514.

MARTINS, F. B. *et al.* Diagnostic accuracy of ultrasonography in relation to salivary gland biopsy in Sjögren's syndrome: a systematic review with meta-analysis. **Dentomaxillofacial Radiology**, v. 53, n. 2, p. 91-102, 2024. DOI: 10.1093/dmfr/twad007.

MOOLA, S. *et al.* Systematic reviews of etiology and risk. In: AROMATARIS, E. *et al.* (Ed.). **JBI Manual for Evidence Synthesis**. JBI, 2024. Disponível em: https://synthesismanual.jbi.global. Acesso em: 07 fev. 2025. DOI: 10.46658/JBIMES-24-06.

MORAES, F. P. *et al.* A morphological post mortem profile in minor salivary glands changes in females. **Journal of Molecular Histology**, v. 56, n. 1, p. 32, 2024. DOI: 10.1007/s10735-024-10306-1.

MOSSEL, E. *et al.* Ultrasonography of major salivary glands compared with parotid and labial gland biopsy and classification criteria in patients with clinically suspected primary Sjögren's syndrome. **Annals of the Rheumatic Diseases**, v. 76, n. 11, p. 1883-1889, 2017. DOI: 10.1136/annrheumdis-2017-211250.

OLIVEIRA, F. R. *et al.* Recommendations on neurologic, cognitive, and psychiatric manifestations in patients with Sjögren's disease by the Brazilian Society of Rheumatology. **Advances in Rheumatology**, v. 65, n. 1, p. 7, 2025. DOI: 10.1186/s42358-025-00438-7.

OLIVEIRA, F. R. *et al.* Clinical and laboratory evaluation of sicca complaints: distinctive aspects of primary, secondary and non-Sjogren syndrome. **Advances in Rheumatology**, v. 62, n. 1, p. 23, 2022. DOI: 10.1186/s42358-022-00255-2.

ORUK, Y. E. *et al.* Effectiveness of ultrasonography and shear wave sonoelastography in Sjögren syndrome with salivary gland involvement. **Ultrasonography**, v. 40, n. 4, p. 584-593, 2021. DOI: 10.14366/usg.21014.

OUZZANI, M. *et al.* Rayyan-a web and mobile app for systematic reviews. **Systematic Reviews**, v. 5, n. 1, 210, 2016. DOI: 10.1186/s13643-016-0384-4.

OXHOLM, P. Primary Sjögren's syndrome--clinical and laboratory markers of disease activity. **Seminars in Arthritis and Rheumatism**, v. 22, n. 2, p. 114-126, 1992. DOI: 10.1016/0049-0172(92)90005-x.

ÖZER, H. *et al.* Diagnostic performance of gray-scale ultrasound and shear wave elastography in assessing salivary gland involvement in patients with primary Sjögren's syndrome. **Journal of Clinical Ultrasound**, v. 51, n. 1, p. 187-194, 2023. DOI: 10.1002/jcu.23379.

PAGE, M. J. *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. **BMJ**, v. 372, n. 71, 2021. DOI: 10.1136/bmj.n71.

PARK, S. Y.; KANG, B. J. Combination of shear-wave elastography with ultrasonography for detection of breast cancer and reduction of unnecessary biopsies: a systematic review and meta-analysis. **Ultrasonography**, v. 40, n. 3, p. 318-332, 2021. DOI: 10.14366/usg.20058.

PRATA, A. R. *et al.* Shear-wave elastography evaluation of major salivary glands in primary Sjögren’s syndrome. **ARP Rheumatology**, v. 1, n. 3, p. 197-204, 2022.

PRICE, E. J. *et al.* British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease. **Rheumatology**, v. 64, n. 2, p. 409-439, 2025. DOI: 10.1093/rheumatology/keae152.

PROCTOR, G. B.; SHAALAN, A. M. Disease-induced changes in salivary gland function and the composition of saliva. **Journal of Dental Research**, v. 100, n. 11, p. 1201-1209, 2021. DOI: 10.1177/00220345211004842.

PSIANOU, K. *et al.* Clinical and immunological parameters of Sjögren's syndrome. **Autoimmunity Reviews**, v. 17, n. 10, p. 1053-1064, 2018. DOI: 10.1016/j.autrev.2018.05.005.

REBEL, D. *et al.* Added value of the salivary gland ultrasonography OMERACT score in the ACR/EULAR classification criteria for Sjögren's disease. **Seminars in Arthritis and Rheumatism**, v. 67, 152473, 2024. DOI: 10.1016/j.semarthrit.2024.152473.

ROBIN, F. *et al.* Diagnostic Performances of Ultrasound Evaluation of Major Salivary Glands According to the 2019 Outcome Measures in Rheumatology Ultrasound

Scoring System. **Arthritis Care & Research**, v. 74, n. 11, p. 1924-1932, 2022. DOI: 10.1002/acr.24631.

SATIŞ, H. *et al.* Parotid elastography: a potential alternative to replace labial biopsy in classification of patients with primary Sjögren's syndrome? **Clinical Rheumatology**, v. 39, n. 12, p. 3707-3713, 2020. DOI: 10.1007/s10067-020-05146-9.

SHIBOSKI, C. H. *et al.* 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for primary Sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. **Arthritis & Rheumatology**, v. 69, n. 1, p. 35-45, 2017. DOI: 10.1002/art.39859.

SHIBOSKI, S. C. *et al.* American College of Rheumatology classification criteria for Sjögren's syndrome: a data-driven, expert consensus approach in the Sjögren's International Collaborative Clinical Alliance cohort. **Arthritis Care & Research**, v. 64, n. 4, p. 475-487, 2012. DOI: 10.1002/acr.21591.

ŚWIECKA, M. *et al.* Shear wave elastography as a potential additional diagnostic tool in primary Sjögren's syndrome: an observational study. **Rheumatology International**, v. 42, n. 9, p. 1579-1587, 2022. DOI: 10.1007/s00296-022-05120-5.

TREVISANI, V. F. M. *et al.* Recommendations from the Brazilian society of rheumatology for the diagnosis of Sjögren's syndrome (Part I): glandular manifestations (systematic review). **Advances in Rheumatology**, v. 59, n. 1, 58, 2019. DOI: 10.1186/s42358-019-0102-8.

TREVISANI, V. F. M. *et al.* Recommendations for evaluation and diagnosis of extra-glandular manifestations of primary Sjögren syndrome: results of an epidemiologic systematic review/meta-analysis and a consensus guideline from the Brazilian society of rheumatology (hepatic, gastrointestinal and pancreatic). **Advances in Rheumatology**, v. 62, n. 1, 35, 2022. DOI: 10.1186/s42358-022-00267-y.

TREVISANI, V. F. M. *et al.* Recommendations for evaluation and diagnosis of extra-glandular manifestations of primary sjogren syndrome: results of an epidemiologic systematic review/meta-analysis and a consensus guideline from the Brazilian Society of Rheumatology (articular, pulmonary and renal). **Advances in Rheumatology**, v. 62, n. 1, 18, 2022. DOI: 10.1186/s42358-022-00248-1.

TURNAOGLU, H. *et al.* Diagnostic value of acoustic radiation force impulse imaging in the assessment of salivary gland involvement in primary Sjögren's syndrome. **Medical Ultrasonography**, v. 20, n. 3, p. 313-318, 2018. DOI: 10.11152/mu-1397.

VAN NIMWEGEN, J. F. *et al.* Incorporation of salivary gland ultrasonography into the American College of Rheumatology/European League Against Rheumatism Criteria for primary sjögren's syndrome. **Arthritis Care & Research**, v. 72, n. 4, p. 583-590, 2020. DOI: 10.1002/acr.24017.

VITALI, C. *et al.* Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. **Annals of the Rheumatic Diseases**, v. 61, n. 6, p. 554-558, 2002. DOI: 10.1136/ard.61.6.554.

WAN, X. *et al.* Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. **BMC Medical Research Methodology**, v. 14, 135, 2014. DOI: 10.1186/1471-2288-14-135.

WIERZBICKA, M. *et al.* Sonoelastography--a useful adjunct for parotid gland ultrasound assessment in patients suffering from chronic inflammation. **Medical Science Monitor**, v. 20, p. 2311-2317, 2014. DOI: 10.12659/MSM.890678.

WISE, C. M. *et al.* Comparison of parotid and minor salivary gland biopsy specimens in the diagnosis of Sjögren's syndrome. **Arthritis & Rheumatism**, v. 31, n. 5, p. 662-666, 1988. DOI: 10.1002/art.1780310512.

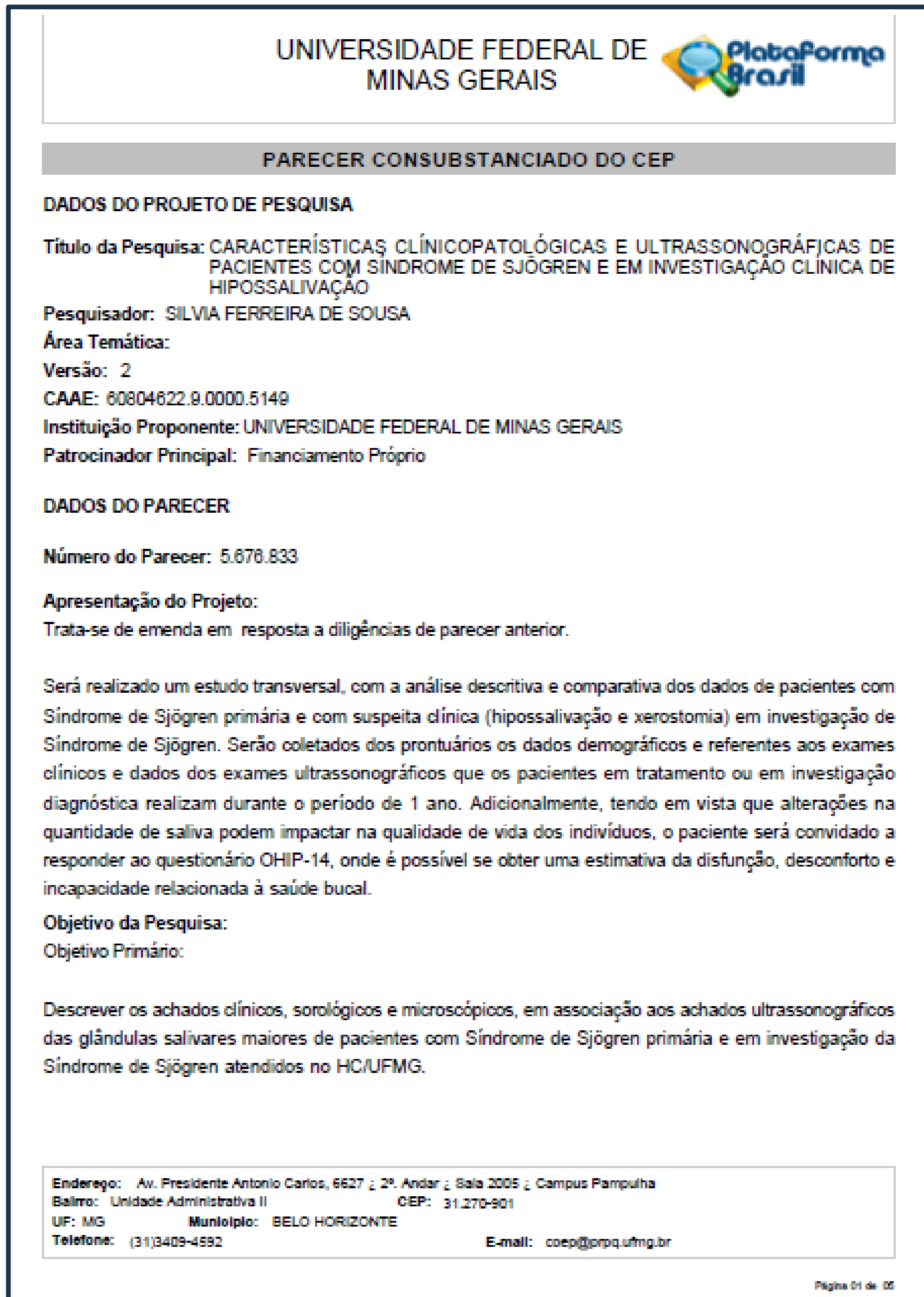
XU, Z. *et al.* Combination of ultra-micro angiography and sound touch elastography for diagnosis of primary Sjögren's syndrome: a diagnostic test. **Quantitative Imaging in Medicine and Surgery**, v. 13, n. 10, p. 7170-7179, 2023. DOI: 10.21037/qims-23-711.

ZANDONELLA CALLEGHER, S. *et al.* Sjögren syndrome: looking forward to the future. **Therapeutic Advances in Musculoskeletal Disease**, v. 14, 1759720X221100295, 2022. DOI: 10.1177/1759720X221100295.

ZHAN, Q. *et al.* Pathogenesis and treatment of Sjogren's syndrome: Review and update. **Frontiers in Immunology**, v. 14, 1127417, 2023. DOI: 10.3389/fimmu.2023.1127417.

ZHANG, M. *et al.* Systematic review and meta-analysis of the diagnostic performance of lacrimal gland ultrasound elastography in primary Sjögren's syndrome. **International Ophthalmology**, v. 44, n. 1, 271, 2024. DOI: 10.1007/s10792-024-03185-8.

APÊNDICE A – Aprovação do Comitê de Ética em Pesquisa



UNIVERSIDADE FEDERAL DE MINAS GERAIS

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: CARACTERÍSTICAS CLÍNICOPATOLÓGICAS E ULTRASSONOGRÁFICAS DE PACIENTES COM SÍNDROME DE SJÖGREN E EM INVESTIGAÇÃO CLÍNICA DE HIPOSSALIVAÇÃO

Pesquisador: SILVIA FERREIRA DE SOUSA

Área Temática:

Versão: 2

CAAE: 60804622.9.0000.5149

Instituição Proponente: UNIVERSIDADE FEDERAL DE MINAS GERAIS

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 5.676.833

Apresentação do Projeto:

Trata-se de emenda em resposta a diligências de parecer anterior.

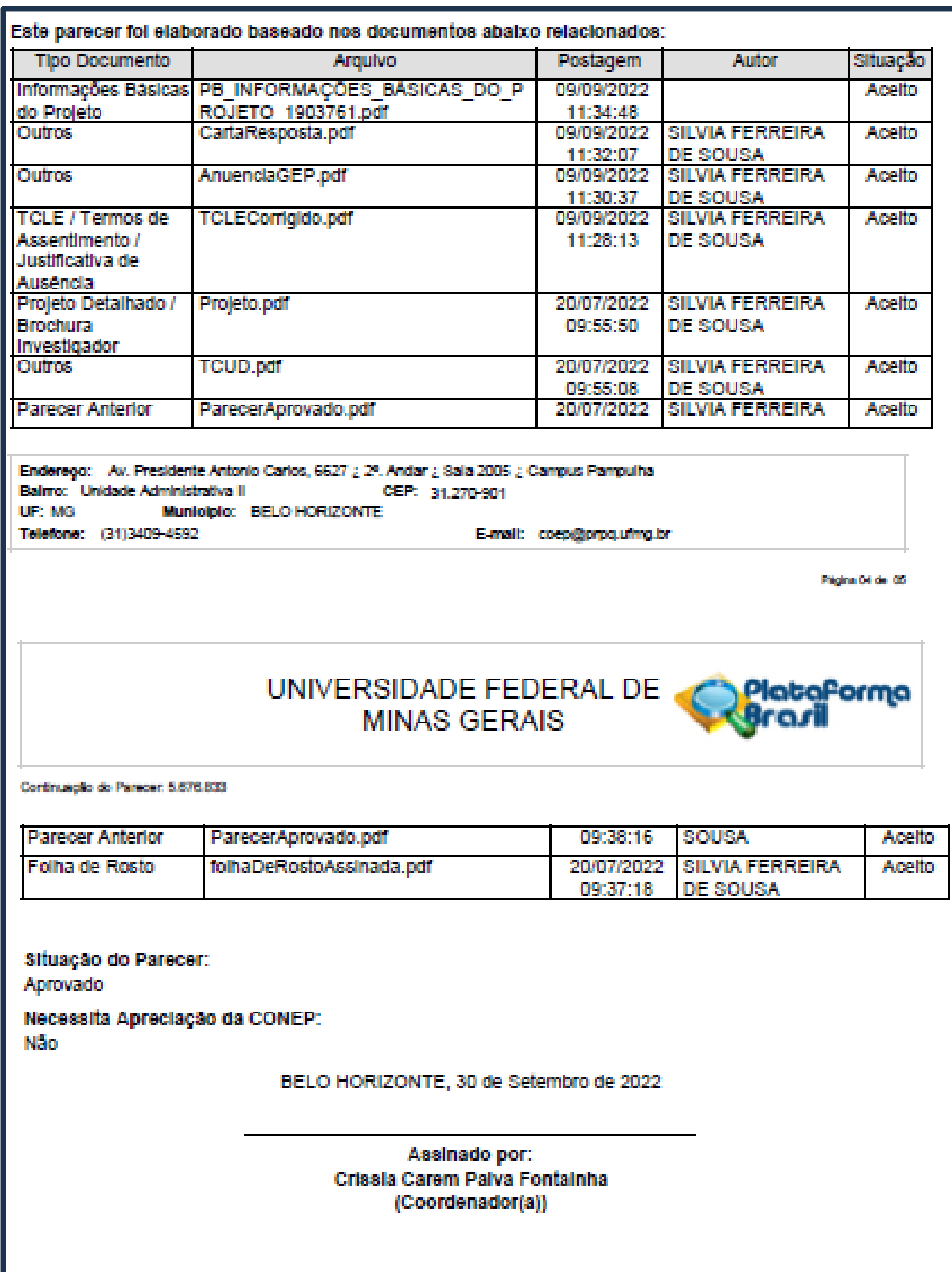
Será realizado um estudo transversal, com a análise descritiva e comparativa dos dados de pacientes com Síndrome de Sjögren primária e com suspeita clínica (hipossalivação e xerostomia) em investigação de Síndrome de Sjögren. Serão coletados dos prontuários os dados demográficos e referentes aos exames clínicos e dados dos exames ultrassonográficos que os pacientes em tratamento ou em investigação diagnóstica realizam durante o período de 1 ano. Adicionalmente, tendo em vista que alterações na quantidade de saliva podem impactar na qualidade de vida dos indivíduos, o paciente será convidado a responder ao questionário OHIP-14, onde é possível se obter uma estimativa da disfunção, desconforto e incapacidade relacionada à saúde bucal.

Objetivo da Pesquisa:

Objetivo Primário:

Descrever os achados clínicos, sorológicos e microscópicos, em associação aos achados ultrassonográficos das glândulas salivares maiores de pacientes com Síndrome de Sjögren primária e em investigação da Síndrome de Sjögren atendidos no HC/UFMG.

Endereço: Av. Presidente Antonio Carlos, 6627 ¿ 2º. Andar ¿ Sala 2005 ¿ Campus Pampulha
Bairro: Unidade Administrativa II **CEP:** 31.270-901
UF: MG **Município:** BELO HORIZONTE
Telefone: (31)3409-4592 **E-mail:** coep@prpq.ufmg.br



Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1903761.pdf	09/09/2022 11:34:48		Aceito
Outros	CartaResposta.pdf	09/09/2022 11:32:07	SILVIA FERREIRA DE SOUSA	Aceito
Outros	AnuenciaGEP.pdf	09/09/2022 11:30:37	SILVIA FERREIRA DE SOUSA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLECorrigido.pdf	09/09/2022 11:28:13	SILVIA FERREIRA DE SOUSA	Aceito
Projeto Detalhado / Brochura Investigador	Projeto.pdf	20/07/2022 09:55:50	SILVIA FERREIRA DE SOUSA	Aceito
Outros	TCUD.pdf	20/07/2022 09:55:08	SILVIA FERREIRA DE SOUSA	Aceito
Parecer Anterior	ParecerAprovado.pdf	20/07/2022 09:38:16	SILVIA FERREIRA SOUSA	Aceito
Folha de Rosto	folhaDeRostoAssinada.pdf	20/07/2022 09:37:18	SILVIA FERREIRA DE SOUSA	Aceito

Endereço: Av. Presidente Antonio Carlos, 6627 ¿ 2º. Andar ¿ Sala 2005 ¿ Campus Pampulha
Bairro: Unidade Administrativa II **CEP:** 31.270-901
UF: MG **Município:** BELO HORIZONTE
Telefone: (31)3409-4592 **E-mail:** coep@prpq.ufmg.br

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

BELO HORIZONTE, 30 de Setembro de 2022

Assinado por:
Crissia Carem Paiva Fontainha
(Coordenador(a))