






# B-Scan Ultrasound Evaluation for Uveitis in Inflammatory Arthropathies: Systematic Review

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## Abstract

The ocular inflammatory process may be associated with autoimmune inflammatory joint damage and can be better recovered by B-mode ultrasound, being little explored in the absent eye evaluation. This study aimed to conduct a systematic review using the Patients or Problem, Intervention, Control or Comparison, Outcomes strategy: uveitis; ultrasound, arthritis, and diagnosis.

Clinical trials, meta-analysis, and randomized controlled trials that specifically address the scope of this study will be evaluated. For the search in the database, a choice of controlled vocabulary will be used with the MEDLINE MeSH platform (Medical Subject Headings). The articles must be dated from the year 2010 until the year 2020. To charting methods will be used Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow Diagram and risk of bias: the Cochrane risk of bias tool. Grade of recommendation assessment: Grading of Recommendations Assessment, Development, and Evaluation Group guidelines.

Of 2909 studies, only 13 studies were included, which evaluated the use of B-mode ultrasound to assess anterior and intermediate uveitis and complications, and 5 cases showed an association of vitreitis.

B-mode ultrasound can be an important benefit of complementing clinical evaluation in patients with the uveal inflammatory process associated with several autoimmune arthropathies, but more studies with better-elaborated methodology design will be necessary.

**Keywords:** ultrasonography, uveitis, arthritis

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**Cite this article as:** Mendonça JA, de Figueiredo Torres Caivano R, Casani Rech I, Siste de Almeida Aoki I, Chagas Cavuto C. B-scan ultrasound evaluation for uveitis in inflammatory arthropathies: Systematic review. *Eur J Rheumatol*. 10.5152/eurjrheum.2023.22054 [Epub Ahead of Print].

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Received: May 15, 2022  
Accepted: January 13, 2023  
Publication Date: April 16, 2023

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## Introduction

### Ocular Anatomy

The eyeball can be anatomically divided into 3 layers, the outermost being called the fibrous layer, which is composed of the sclera, cornea, and the corneal scleral junction (also called corneal sclero limbus). This part is composed of dense tissue, homologous to the *dura mater* of the central nervous system and is poorly vascularized. On the other hand, the intermediate or vascular layer is represented by the uvea, which corresponds to a continuous structure formed by the anterior (iris and ciliary body), intermediate (vitreous humor), and posterior (choroid) portions. The inner or sensorineural layer is composed of the retina, whose main elements are the photoreceptors, ganglion, and bipolar cells.<sup>1</sup>

### Ocular Ultrasonography

Ocular ultrasound has gained space within the evaluation of ophthalmic lesions due to its characteristics as non-invasive method, easily reproduced, which does not pose great risks to the patient and because it is more accessible than other imaging methods. In general, ophthalmic equipment is set to a frequency close to 8 MHz or above, which allows penetration into ocular tissues.

The use of ultrasound in ocular assessment has different indications, including the study of the anterior and posterior segments, in addition to the characterization of vascularization and biometry.<sup>2</sup> Indications for evaluation can be divided into pathologies with opacification of the ocular middle layer or not. In cases of opacification, the main changes evaluated are corneal opacification, hyphema, small pupil, cataract, and hemorrhage or vitreous inflammation. On the other hand, pathologies that will require an ultrasound study and that do not present with opacification can be represented by injury of the iris, lesions of the ciliary body, tumors, detachment of the retina, optic nerve abnormalities, analysis of the extraocular muscles

and orbit, intraocular foreign body detection, ocular trauma follow-up, iridocorneal angle follow-up, and biometry.<sup>2</sup>

As it is a minimally invasive technique that presents minimal risks to the patient, the use of ultrasound has few contraindications, among which it is worth mentioning suspected rupture of the eyeball, especially in patients who have suffered trauma or who have recently undergone surgery. The ocular ultrasound evaluation is performed with the eyes closed, using a large amount of gel and without pressing the structures; this is a dynamic exam, asking the patient to move the eye lateromedially, with the probe positioned longitudinally or transversally.<sup>3</sup>

The most used is B-mode ultrasound, which simultaneously transmits multiple sound waves through the transducer at different angles (each corresponding to an A-mode wave). By combining the 2 modalities, it is possible to compose a 2-dimensional image of the assessed tissue.<sup>2</sup>

Ultrasonography consists of a dynamic evaluation method, allowing the interpretation of results according to the evolution of the images throughout the exam, in addition to static evaluation.<sup>2</sup>

The examination must follow a predetermined sequence for the correct assessment of ocular integrity. Topography is essential to locate and determine the shape of any abnormality, being performed before the quantitative evaluation of reflectivity, attenuation and structure of any lesion. Finally, the kinetic evaluation will determine the mobility of the structures and if pathological or not.<sup>2</sup>

It is essential to systematically scan the eyes to determine changes. The high gain of this imaging method is initially used in order to visualize the vitreous cavity, being reduced according to the need for evaluation of the retina, choroid, and solid lesions.<sup>2</sup> The protocol requires obtaining images in the axial section of the entire eyeball, from the superior to the inferior pole, and of sagittal images from the temporal to nasal portion. Oblique and dynamic images can be obtained by carefully moving the eyes from right to left and from top to bottom.<sup>3</sup>

Therefore, the ultrasound examination is composed of 3 basic assessments: topographic, which includes location, extension, and shape of structures; quantitative, evaluating the ocular internal structure and reflectivity (usually

requiring the use of mode A), and the kinetic evaluation, presenting data after eye movement and on vascularization.<sup>2</sup>

### Ocular Ultrasound Assessment in Arthritis

#### Patients

Ultrasonography is an imaging method that has been reported in different studies due to its ability to assess joint inflammatory processes, currently considered safe to be used routinely in this area. In addition, it is an imaging modality capable of generating excellent images of the anterior uvea, vitreous cavity, and peripheral retina in normal eyes or eyes affected by inflammatory processes, such as intermediate uveitis. Still little explored and not validated for frequent use as a diagnostic method and treatment monitoring, in some cases, it stands out for its practicality and reliability in the joint assessment of other pathologies, especially inflammatory joint diseases.<sup>2-5,19</sup>

#### Methods

This review was carried out in accordance with the recommendations of the Cochrane Collaboration.<sup>7</sup> Before starting this systematic review, it was registered with Prospero (International prospective register of systematic reviews), obtaining registration CRD42021248376. For the clinical question, which guided this work, the Patients or Problem, Intervention, Control or Comparison, Outcomes (PICO)<sup>25</sup> strategy was used: Patients: patients with uveitis; Intervention: evaluation with ultrasound; Comparison: patients with and without arthritis; Outcomes: diagnosis and follow-up of uveitis. Thus, through a systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses methodology,<sup>6</sup> we sought to study the use of ultrasound in uveitis for diagnosis and follow-up, especially in patients with arthritis.

A systematic review of the current literature was carried out using the MEDLINE database through PubMed, with the objective of identifying studies that contained data on the use of ultrasound to evaluate uveitis cases, especially in the framework of patients with concomitant arthritis, in which it was unheard subject at that time. To search the database, a controlled vocabulary was selected using the MEDLINE MeSH (Medical Subject Headings) platform. The research was carried out with results obtained after the protocol submission and the entire process was reviewed by 3 readers and the critical analysis of the whole content by the other authors. Search key words were developed with the assistance

of the MeSH terms and included "uveitis," "anterior," "posterior," "intermediate," "pars planitis," "ophthalmia," "panuveitis," "diagnostic," "diagnosis," "diagnoses," "procedures," "techniques," "ultrasound," "ultrasonography," "medical sonography," "imaging," "ultrasonographic," "arthritis," "arthritides," "polyarthritis," "polyarthritides," "outcome and process assessment," and "symptom assessment."

Initially, 2909 studies were found. However, for both studies, only articles written in English, published in the last 10 years, and reported in the MEDLINE database were considered eligible.

For the first search in the database, we used the PICO strategy with the additive "OR" and "AND" in the PubMed database, using as "control" the inflammatory joint pathologies called "arthritis," which restricted the search to 296 results; only 251 articles were in English and 119 were published in the last 10 years. Cross-sectional, clinical trials, and observational scientific articles covering the study subject were evaluated. Pictorial reviews, systematic reviews, reviews, and meta-analysis were excluded as they did not fit the survey scope. In addition, the entire research was reviewed by the 3 readers. Clinical trials in any phase and study design were excluded due to dissociation with the survey subject after the 3 readers reached consensus. Thus, after applying the inclusion criteria: scientific articles such as case report, cross-sectional study, original articles, non-randomized and randomized clinical trials, articles published less than 10 years before, and English language, 68 studies were excluded by reading the title, 21 by reading the abstract, 30 articles were read in full, selecting 3 of them.

The second research aimed to cover a greater number of studies on the use of ultrasound as a method of monitoring and evaluating inflammatory diseases of the uveal tract, removing the descriptors for comparison. Thus, a total of 2613 studies were obtained, 2187 in English, and 1146 published in the last 10 years; 1087 articles were found in the MEDLINE platform and 1063 studies were related to humans. Thus, after applying the previously mentioned inclusion criteria, 844 articles were excluded by reading the title and 73 by reading the abstract; 146 publications were read in full and 8 of them were selected.

After the aforementioned research, 8 articles were manually included; they were selected because they were closely related to the

research scope; however, 3 of them were excluded because they had been published more than 10 years before and 3 because they were review articles. Thus, 2 more articles were included.

### Assessment of Bias and Grade of Recommendation

The Critical Assessment Tool through the Cochrane Risk of Bias Tool for Studies Reporting Prevalence Data<sup>7</sup> was applied to all the studies included. In terms of structure and sampling, most studies used a clinical approach and included patients who had ocular pathologies that could be evaluated by ultrasound, among other methods of ocular imaging. The sample sizes ranged from 1 to 243, and all were based on convenience, without clearly indicating a sample size calculation logic. Study subjects were adequately described in all the studies included, and valid methods to determine the presence of the pathological condition were used and most of them were described. Overall, the risk of bias was assessed as moderate to critical due to the small sample size of the studies and non-randomization in patient selection.

To assess the degree of recommendation and level of evidence, the strategy proposed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Group<sup>24</sup> was used, evaluating the use of B-mode ultrasound for anterior and intermediate uveitis, and the use of ultrasound imaging method for ocular complications, which may result from the inflammatory processes evaluated by this study. To this end, original articles and case reports that were part of the subject in question were analyzed.

### Results

Initially, a total of 2909 studies were found; however, after applying the inclusion criteria, 11 studies were selected for this review. In addition, 2 more articles were manually included, resulting in a total of 13 articles reviewed (Figure 1).

### Main Findings of the Studies Included

It was possible to identify different methodologies and variables after a thorough analysis of the 13 articles included in the review. The main and most relevant data for this systematic review were summarized in Table 1. It was not possible to combine the data and compare them due to the methodological variability of the studies. The Risk of Bias in Non-randomized Studies of Interventions<sup>26</sup> tool was used, but the studies had different methodological flaws

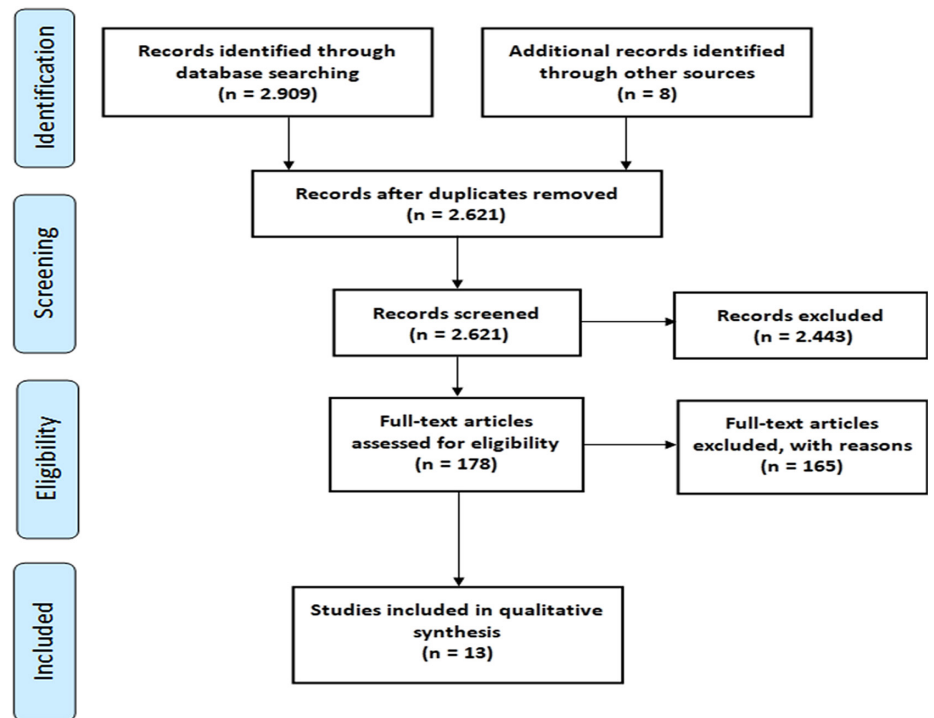


Figure 1. Flow chart of the literature screening process.

in relation to confounding bias, selection bias, information bias, reporting bias, etc. (Figure 2). Regarding the risk of bias, most studies in the domains, in general, had a judgment with high risk of bias, but in bias to missing data, all studies obtained a judgment with a low risk of bias (Figure 3).

### Ultrasonographic Assessment of Ocular Inflammatory Diseases

Most studies that were evaluated with the objective of diagnosing inflammatory ocular manifestations through ultrasound corresponded to case reports. Due to the great methodological variability of the sample of articles, it was not possible to group the data and establish standards with statistical evaluation.

The assessment of inflammatory activity through ultrasound was performed in 11 studies (Table 2). Only 4 of the articles detailed the technology used, and it is important to highlight the use of the linear transducer in B-mode with high frequency, varying between the studies of 7.5 and 20 MHz.<sup>4,5,9,10</sup>

The technique of performing the ultrasound examination was described in 4 studies: the use of a significant amount of gel on the eyelid of the globe to be evaluated and the transpalpebral contact are important measures necessary to perform the diagnostic procedure correctly.<sup>4,5,9,10</sup>

However, it is possible to assess the close relationship between these inflammatory pathologies and predisposing ocular alterations, such as glaucoma (especially in cases with a closed angle)<sup>8,12</sup>, and the concomitance of other infectious and inflammatory pathologies, especially linked to autoimmunity, such as arthritis.<sup>4,5,16</sup> As evidenced by Yang et al.<sup>16</sup> panescleritis was associated with greater involvement by systemic and local diseases ( $P = .001$ ), especially tuberculosis ( $P = .009$ ).

Corroborating what had previously been mentioned, Morais et al.<sup>10</sup> evaluated 47 patients with active ocular toxoplasmosis, with changes in the vitreous humor of all patients, an important differential diagnosis in relation to the uveal inflammatory process in arthropathies, which can be evaluated with ultrasound, considering a detailed clinical history.

Despite appearing to be useful in the anatomical assessment of ocular structures, sometimes inflammatory pathologies may not present changes detectable by the ultrasound technique,<sup>13,17</sup> requiring the use of other imaging tests to perform the diagnosis.

As illustrated in Table 3, the level of evidence and degree of recommendation for the use of B-mode ultrasound for ocular assessment in anterior and intermediate uveitis was analyzed, but ultrasonographic assessments of posterior uveitis were not described in the selected

Table 1. Studies Included

Author	Year	Study Design	Sample Characteristics	Aim	Ultrasonography Assessment	Ultrasonography Variables Reported
Mendonça et al <sup>4</sup>	2021	Case report	Male patient, 47 years old, Caucasian, diagnosed with spondyloarthritis for 12 years with negative HLAB27. The patient was affected by redness of the eye on the left (free of uveitis by ophthalmologic evaluation) concomitant with arthritis in the right shoulder and knee in the last 6 months. The patient had already used infliximab, adalimumab, and had been using etanercept for the last year. Certolizumab 400 mg weekly was started at weeks 0, 2, and 4, with an induction dose.	Use ultrasound with a high-frequency linear transducer to monitor the effects of certolizumab treatment in a patient with HLAB27-negative uveitis and spondyloarthritis.	A B-scan ultrasound of the MyLab 25 Gold ultrasound (Esaote SpA, São Paulo, Brazil) with 12 MHz high-frequency linear probe, with a PD frequency of 6.6 to 8 MHz, pulse repetition frequency that varied from 0.5 Hz to 1.0 MHz and low filter, performed by a single rheumatologist with 12 years' experience. Technique: eyes closed, sufficient gel and no structures compression. Dynamic assessment with transducer positioned longitudinally, asking to move the eyes lateromedially.	Presence of hypoechoic fluctuating images in the vitreous humor of the left eye, showing a reduction of the same after 7 months of treatment.
Mendonça et al <sup>5</sup>	2020	Case report	Female patient, 32 years old, Caucasian, without previous diagnosis. Eye erythema when using computer, nail pitting, and arthritis in left knee for 6 months.	Use ultrasound with a high-frequency linear transducer to detect ocular and joint inflammatory changes in a patient with no previous diagnosis.	A B-scan ultrasound of the MyLab 50 linear transducer (Esaote SpA., São Paulo, Brazil) with 12 MHz high-frequency linear probe performed by a single rheumatologist with 12 years experience. Technique: eyes closed, sufficient gel and no compression of structures. Dynamic evaluation with transducer positioned transversely and longitudinally, asking to move the eyes lateromedially.	Fluctuating confluent hypoechoic images in the vitreous humor, more intense on the left, and sparse hypoechoic images on the right. Diagnosis: vitritis (intermediate uveitis).
Alsarhani et al <sup>22</sup>	2020	Case report	Male patient, 25 years old, with eye pain associated with redness and reduced visual acuity for 2 days.	To report a case about nodular posterior scleritis and the multiple imaging methods that can be used to aid diagnosis, reviewing the literature on the subject.	B-scan and A-scan ultrasound, with no mention of equipment specifications.	B-mode ultrasound showed subretinal fluid and hyperechoic nodular scleral thickening, with diffuse edema below Tenon's space. A-mode ultrasound showed that the lesion had average internal reflectivity.
Kumar et al <sup>23</sup>	2019	Case report	Male patient, 12 years old, with pain, redness, and reduced visual acuity in the left eye for 10 days. History of right hip pain and fever for 20 days. After investigation with laboratory and imaging tests, the diagnosis of enthesitis-related arthritis, a form of juvenile idiopathic arthritis, which was associated with severe intermediate uveitis, was suggested.	To report a case of juvenile idiopathic arthritis related to uveitis, mimicking endophthalmitis.	B-scan ultrasound, no mention of equipment specifications.	The evaluation with B-mode ultrasound showed amplitude peaks leading to moderate in the vitreous cavity, suggestive of vitreous exudate.

(Continued)

**Table 1.** Studies Included (*Continued*)

Author	Year	Study Design	Sample Characteristics	Aim	Ultrasonography Assessment	Ultrasonography Variables Reported
Bromeo and Bartilad <sup>8</sup>	2019	Case report	Female patient, 36 years old, complaining of bilateral eye pain, more intense on the right, as well as reduced visual acuity in the right eye, for 1 month.	To report in detail the management of nanophthalmia in a patient who presented a complication with angle-closure glaucoma, and anterior uveitis. Nanophthalmos is a condition in which the eye is shortened (axial length <19 to 21 mm), so that the lens becomes proportionally enlarged compared to the ocular volume, associated with hypermetropia and choroidal or scleral thickening, with bilateral involvement.	B-scan ultrasound, no mention of equipment specifications. Among the methods, the following stand out: fluorescein angiography and perimetry—performed with the Octopus Visual Field Analyzer.	In both eyes, the imaging exam showed a decreased axial length of the eyeball, 17 mm in the right eye and 16.2 mm in the left eye, associated with a thickening of the choroid. Vitreous humor without opacities and retina without detachments. The most significant finding for uveitis in B-mode US would be choroidal thickening. Diagnosis: nanophthalmos, angle-closure glaucoma, and anterior uveitis in both eyes
Wu et al <sup>9</sup>	2019	Case report	Female patient, 60 years old, complaining of eye pain and reduced visual acuity in the right eye for more than 1 month after placement of intraocular lenses.	To report the use of dynamic ultrasound assessment to diagnose uveitis–glaucoma–hyphema syndrome, which can result in anterior chamber hemorrhage.	B-ultrasound scanner (MyLab Z5, Genoa, Italy) B-ultrasonography (Vinno G60, Suzhou China) in horizontal, sitting, and head-down positions. UBM (Suor SW-3200L, Tianjin, China). Technique: the eyes were checked twice in the horizontal position, sitting, and with the head down, evidencing the movement of the intraocular lenses according to the position.	Vitreous humor opacity, absence of retinal detachment, absence of friction between the intraocular lens and ciliary bodies/iris, and bilaterally open anterior chamber angles were demonstrated in static evaluation. The presence of hyperechoic granular echo granules in the anterior right chamber was also observed in static evaluation. In the dynamic evaluation, performed 1 month after the proposed treatment, ultrasound was performed in both eyes, with a change between the horizontal, sitting, and head-down positions. Thus, it was found that the intraocular lenses were not in contact with the iris pigment epithelium in the horizontal position of both eyes and in the left eye with the head down; however, contact between the intraocular lenses and the iris was evidenced in both eyes in the sitting position and in the right eye with the head down. Diagnosis: uveitis–glaucoma–hyphema syndrome.

(Continued)

Table 1. Studies Included (Continued)

Author	Year	Study Design	Sample Characteristics	Aim	Ultrasonography Assessment	Ultrasonography Variables Reported
Morais et al <sup>10</sup>	2018	Original article	47 patients/eyes with active ocular toxoplasmosis were evaluated. Of these, 22 (46.8%) were female and 25 (53.2%) were male. The mean age was 36.5 years (range, 14-79 years). Median time to onset of symptoms was 16 days. Previous episodes of ocular toxoplasmosis were observed in 21 (44.7%) patients, with a mean recurrence of 1.86 episodes (so that the number of recurrences among the 22 patients involved ranged from 1 to 6 episodes).	To evaluate the sonographic findings associated with active ocular toxoplasmosis.	B-mode, 10-MHz transducer; Alcon, Fort Worth, TX, USA. Ultrasonographic evaluation was performed by a single examiner, using the technique of transpalpebral contact with conductive gel. Parameters evaluated: vitritis (speckled echogenicity in the vitreous proximal to the lesion or diffuse), posterior vitreous detachment (partial or total), posterior hyaloid membrane (thickening and/or adherence to the lesion), vitreoschisis (vitreous detachment), localized choroidoretinal edema, choroidoretinal lesions, and perilesional retinal detachment.	The main ultrasound findings reported were vitritis, posterior vitreous detachment (partial and total), vitreoschisis, choroidoretinal thickening, and perilesional retinal detachment.
Ma et al <sup>11</sup>	2018	Case report	Female, Caucasian, 44 years old, with a previous history of inflammatory arthritis, diffuse erythematous rash and hives, and hearing loss. History of chronic iritis in the right eye, without specifying the time of the signs.	To report a case of uveitis and papillitis in a patient with cryopyrin-associated periodic syndrome.	B-scan ultrasonography, with no mention of equipment specifications.	Elevated optic disc head, with more pronounced swelling on the right side than on the left. Diagnosis: bilateral papillitis and uveitis.
Mahendradas et al <sup>12</sup>	2018	Case report	Female, 36 years old, history of visual acuity loss for 2 days. She was on topiramate for migraine (100 mg per day).	To report a case of eye pain, photophobia, erythema, and sudden reduction of visual acuity in a patient who used topiramate for migraine.	Ultrasonography B-scan and ultrasound biomicroscopy, with no mention of equipment specifications.	In the right eye, vitritis was observed, but in the left eye, low to medium reflective echoes in the vitreous were evaluated, with a retinochoroidal thickening of 1.83 mm. Diagnosis: panuveitis and angle-closure glaucoma in both eyes.
Boricean et al <sup>13</sup>	2017	Case report	Female, 49 years old, history of recurrent panuveitis in the left eye. Complaint of reduced visual acuity, photophobia and floaters in the right eye for 7 days.	To present the difficulties in establishing the diagnosis and treatment in a case of multifocal choroiditis and panuveitis in a patient with paranoid schizophrenia treated with aripiprazole.	B-scan ultrasound, with no mention of equipment specifications.	The examination did not show specific pathological changes in the right eye; however, it showed total retinal detachment in the left eye. Diagnosis: recurrent panuveitis in the left eye associated with multifocal choroiditis and panuveitis in the right eye.

(Continued)

**Table 1.** Studies Included (Continued)

Author	Year	Study Design	Sample Characteristics	Aim	Ultrasonography Assessment	Ultrasonography Variables Reported
Deanehan et al <sup>14</sup>	2017	Case report	Boy, 9 years old, history of intraocular injection 1 month ago. Complaint of reduced visual acuity in the left eye with progressive worsening.	To present a case of pars planitis diagnosed through point-of-care ultrasound.	Evaluation through point-of-care ultrasound performed by a professional with a fellow in pediatric emergency medicine. Use of the FOVEA protocol, described by Kilker et al <sup>15</sup> to evaluate the main ocular structures such as the anterior chamber of the eye, optic, vitreous, extraocular nerves, and vascularization. The FOVEA protocol consists of a schematic eye scan at the bedside, in which the investigation follows the "Front of the eye" sequence (assess the presence of a foreign body, lens dislocations/subluxations, afferent pupillary defects, and changes in chamber size anterior), "Optic nerve" (investigates increased intracranial pressure), "Vitreous" (searches for hemorrhage and/or retinal and/or vitreous detachment, endophthalmitis, and lens displacement), "Extraocular" (searches for the presence of retrobulbar hemorrhage, rupture of the eyeball, foreign bodies) and, finally, "Artery/vascular" (analyzes whether there is occlusion of the central retinal artery or central retinal vein). Technique with a linear high-frequency transducer, patient in a supine or sitting position, eyes closed, transparent plastic sheet over the eyes and enough gel to avoid contact with the eyelids.	Right eye: normal cornea, lens, anterior chamber, vitreous body, and posterior chamber. Left eye: fine hyperechoic cords with free movement in the posterior vitreous cavity, centrally anchored to the optic nerve by a rod (usually anchored in the ora serrata laterally). Diagnosis: pars planitis (intermediate uveitis) and retinal detachment.

(Continued)

Table 1. Studies Included (Continued)

Author	Year	Study Design	Sample Characteristics	Aim	Ultrasonography Assessment	Ultrasonography Variables Reported
Yang et al <sup>16</sup>	2016	Original article	124 men and 169 women. Anterior scleritis in 243 and posterior in 42, the remaining 8 had both conditions. Mean age of 39.4 years. Several other pathologies were detected in 39 (13.3%) patients with scleritis so that 11.6% (n=34) of the patients had autoimmune diseases and 2% (n=6) had infectious diseases. In general, the presence of rheumatoid arthritis was found in 13 cases, ankylosing spondylitis in 10, gout in 4, relapsing polychondritis in 4, and inflammatory bowel disease in 2. In addition, 5 patients had a history of already treated pulmonary tuberculosis, 1 patient had inactive leprosy, there was 1 case of granulomatosis with polyangiitis and 2 cases of inflammatory pseudotumor. Finally, 2 of the patients exhibited concomitant ankylosing spondylitis and relapsing polychondritis and 1 patient had rheumatoid arthritis along with tuberculosis. Scleritis was controlled in 94.6% of patients treated with corticosteroids combined with immunosuppressive agents.	To characterize the clinical findings of Chinese patients with scleritis.	B-mode US and biomicroscopic ultrasound.	Anterior scleritis: retinal detachment, vitreous opacity. Posterior scleritis: posterior wall thickening, fluid below Tenon's capsule, retinal detachment, choroidal detachment, and vitreous opacity. Panescleritis: posterior wall thickening, fluid below Tenon's capsule, choroidal detachment, and vitreous opacity.
Cordero-Coma et al <sup>17</sup>	2011	Cross-sectional	4 cases of posterior scleritis. 50% of female patients mean age 56 years (so the study included patients aged 49 to 72 years).	To report 4 cases of posterior scleritis in which, atypically, 3 of these showed only papillitis as an ultrasound finding and 1 case did not present any abnormality on ultrasound examination, the diagnosis being based on magnetic resonance imaging. Among the evaluated patients, active tuberculosis was detected as a potential cause of scleritis in 1 of the cases and 1 case with a previous history of non-arteritic anterior ischemic optic neuropathy; however, the other cases did not indicate possible causes for the presence of scleritis.	In 3 of the 4 cases evaluated, the only sonographic alteration found was the presence of papillitis, with the T sign (fluid inside the Tenon's capsule and in the optic nerve sheath) being absent in all cases. The case that did not present papillitis as an ultrasound finding had no change detected by B-mode ultrasound. Diagnosis: posterior scleritis: (determined by MRI, as the cases presented did not demonstrate changes related to posterior scleritis on B-mode ultrasound).	



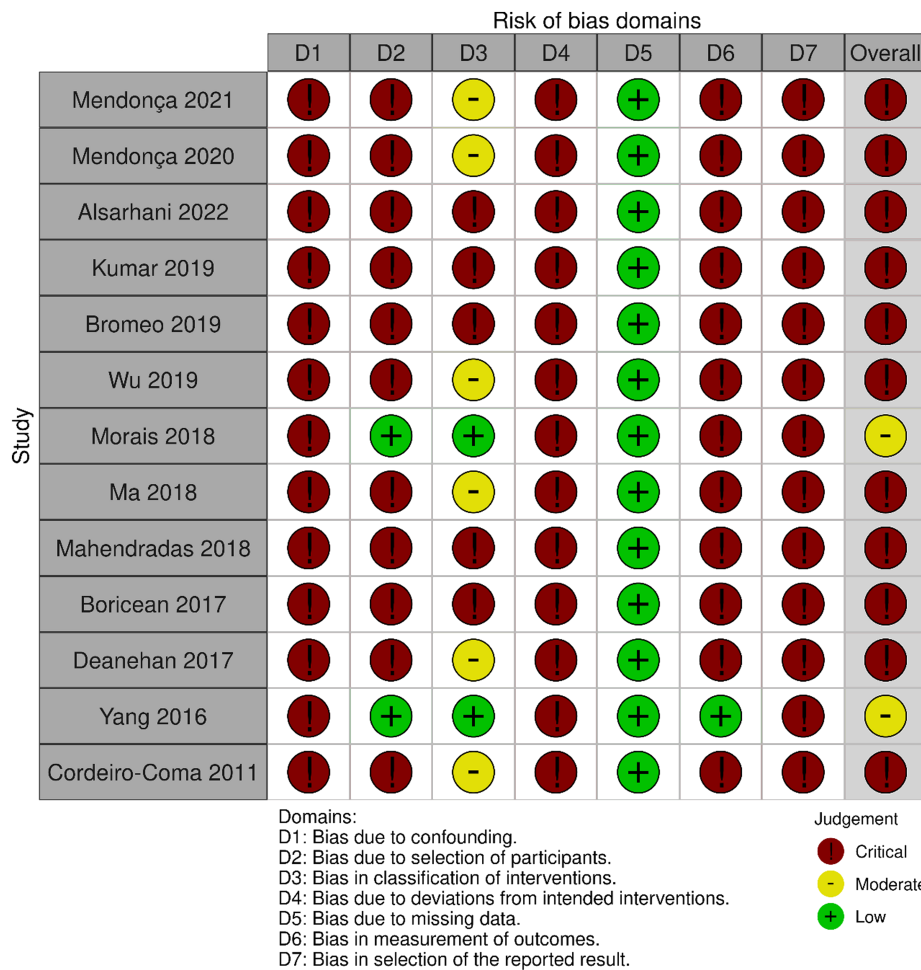


Figure 2. Risk of bias.

studies. To this end, the strategy proposed by the GRADE Group<sup>24</sup> was used, showing that due to the weak methodological description of the studies, as well as the difficulty in evaluating factors such as inconsistency, imprecision and the degree of information provided indirectly (which do not respond directly to the study issue). Thus, a very low level of evidence was observed.

**Ultrasonographic Assessment of Ocular Complications**

By observing the data obtained from the ultrasound imaging evaluation of ocular

complications (Table 2), it is possible to separate these results into 3 groups, which can be identified by vitreous opacity, thickening of ocular structures, and detachment/delamination of structures.

Among the articles reviewed, only 2 described vitreous opacity using the ultrasound technique.<sup>10,16</sup> All studies presented characteristics and diagnosis of retinal, choroidal, or posterior vitreous detachment<sup>10,13,14,16</sup>; however, based on the 2 original articles,<sup>10,16</sup> one might think that there is a tendency to the thickening of ocular structures to be more common than the

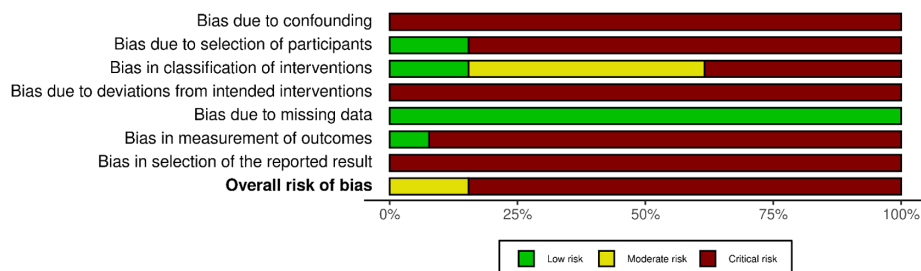


Figure 3. Risk of bias with the percentages in each domain.

detachment of those structures, although this was not uncommon in the patients assessed.

The GRADE Group strategy<sup>24</sup> was used to assess the level of evidence and the degree of recommendation in this item. The level of evidence determined was very low, mainly due to the weak methodological description of the studies, as well as the difficulty in evaluating factors such as inconsistency, imprecision. This is mainly due to the lack of randomized studies, small samples, and very heterogeneous development scenarios, characterizing very different effect estimates (Table 3).

**Discussion**

This systematic review was conducted with the aim of evaluating what the current literature helps adding knowledge about the use of the ocular ultrasound technique to assess the inflammatory condition of ocular structures in the framework of patients who present with some degree of concomitant inflammatory joint involvement. However, it was not possible to carry out a comparative study with data clustering due to the great methodological heterogeneity of the studies found.

It is extremely important to analyze the applicability of ultrasound as a method of investigation, diagnosis, and follow-up, due to its characteristics such as fast exam time, being reliable, safe, low cost, free from radiation, providing excellent real quality images on time, allow dynamic evaluation, be the option of choice in rural centers, rare contraindications, useful in the framework of preoperative planning and allowing evaluation of the posterior segment when the middle layer is opaque.<sup>2,3,10,14,18,19</sup>

Despite being a method not yet validated for routine use without the need for additional evaluation, ultrasound evaluation has shown a satisfactory performance in the identification of several ocular pathologies, especially in the involvement of the vitreous humor and the posterior chamber. Some cases, however, require more attention and a more specific imaging investigation, due to the absence of alterations by this method.<sup>17</sup> The studies selected to compose this systematic review focused on altered parameters, which could suggest the existence of ocular pathology, allowing, in most cases, confirmation of the diagnosis.

A secondary finding evaluated in this review was the characterization of the main complications of these ocular inflammatory processes,

**Table 2.** Ultrasonographic Assessment of Ocular Inflammatory Diseases

Studies	Result	Associated Diseases/Manifestations	Ultrasound Changes	Complications
Mendonça et al	Fluctuating hypoechoic images in the vitreous humor of the left eye, which receded after 7 months of treatment.	Spondyloarthropathy with synovitis in the right shoulder and tenosynovitis of the right posterior tibial tendon.	—	—
Mendonça et al	Fluctuating hypoechoic images confluent in the vitreous humor more intense on the left and sparse hypoechoic images on the right. Diagnosis of vitritis (intermediate uveitis).	Psoriatic arthritis without skin lesions.	—	—
Asarhani et al	Subretinal fluid and hyperechoic nodular scleral thickening, with diffuse swelling below Tenon's space on B-mode ultrasound and mean internal reflectivity on A-mode ultrasound.	Not applicable.	Subretinal fluid on B-mode ultrasound evaluation, diffuse edema in Tenon's space with nodular thickening in the macula.	Retinal detachment with chorioretinal folds in the macula.
Kumar et al	Small to moderate amplitude peaks in the vitreous cavity, suggestive of exudate.	Juvenile idiopathic arthritis, enthesitis-related arthritis subtype.	—	—
Bromeo and Bartilad	A-mode ultrasound evaluation showed ocular axial length of 17 and 16.2 mm in the right and left eyes, respectively. Evaluation in B-mode evidenced relatively short eyeballs, clear vitreous, attached retina, and increased choroidal thickness. Diagnosis: nanophthalmos and bilateral anterior uveitis.	Nanophthalmos with secondary angle-closure glaucoma, and uveal effusion syndrome complicated with bilateral anterior uveitis.	—	—
Wu et al	B-mode ultrasound evaluation demonstrated intraocular lens centered in the scleral pocket and vitreous opacity. The eyes were checked twice in the horizontal, sitting, and upside-down positions; evidencing the movement of the intraocular lenses according to the position. Diagnosis: dynamic interactions between the intraocular lens and the iris/ciliary body indicated the diagnosis of uveitis—glaucoma—hyphema syndrome.	Intraocular lenses in both eyes.	-	-
Morais et al	B-mode ultrasound evaluation showed punctual echogenicities in the vitreous humor of the 47 eyes evaluated (100%), out of which 40 (85.1%) were diffuse and 7 (14.9%) were localized. Diagnosis: vitritis (intermediate uveitis) and toxoplasmic retinochoroiditis. Probably 12 eyes had complications from posterior uveitis secondary to toxoplasmosis, inducing alterations such as thickening of the hyaloid membrane and adhesions to the exudative focus, which could lead to partial/total vitreous detachment.	All 47 patients/eyes evaluated had active ocular toxoplasmosis.	B-mode ultrasound evaluation showed punctual echogenicities in the vitreous humor, posterior vitreous detachment, and hyaloid thickening. Vitreous detachment with adherence of the hyaloid to the exudative lesion, but ultrasound was not able to differentiate alterations in the contours of the lesions. Vitreoschisis and total posterior vitreous detachment.	Total of 47 eyes/patients evaluated: - Posterior vitreous detachment in 36 (76.6%), with 35 (97.2%) showing hyaloid thickening and 4 (11.1%) adherence to the exudative lesion - Partial posterior vitreous detachment in 12 (25.5%) - Total posterior vitreous detachment in 23 (48.9%) - Vitreoschisis in 12 (25.5%) - Choroidoretinal thickening in 12 (25.5%) - Perilesional non-regmatogenous retinal detachment in 5 (10.6%)

(Continued)

**Table 2.** Ultrasonographic Assessment of Ocular Inflammatory Diseases (*Continued*)

Studies	Result	Associated Diseases/Manifestations	Ultrasound Changes	Complications
Ma et al	B-mode ultrasound evaluation showed optic disc elevation associated with edema with the right side worse than the left. Diagnosis: uveitis and papillitis associated with cryopyrin-associated periodic syndrome (CAPS).	Inflammatory arthritis, chronic iritis in the right eye, CAPS.	—	—
Mahendradas et al	B-mode ultrasound evaluation showed bilateral vitritis and low to medium reflective echogenicity in the vitreous with retinochoroidal thickening of 1.83 mm. B-mode ultrasound was performed again on the left eye and showed fluid below Tenon's capsule and retinochoroidal thickening of 1.76 mm.	Acute bilateral angle-closure glaucoma secondary to the use of topiramate, which generated bilateral panuveitis and vitritis in the left eye. Left eye developed multiple posterior synechiae with complicated cataract.	—	—
Boricean et al	There were no changes, but the patient was diagnosed with multifocal choroiditis and panuveitis.	Antipsychotic-related chorioretinopathy and Birdshot-like syndrome were not excluded.	B-mode ultrasound evaluation showed total retinal detachment in the left eye, but no pathological changes in the right eye.	Patient diagnosed with multifocal choroiditis and panuveitis through different imaging tests (optical coherence tomography, angiofluorography, B-mode ultrasound) and fundoscopic examination.
Deanehan et al	Right eye: normal cornea, lens, anterior chamber, vitreous body, and posterior chamber. Left eyes: thin hyperechoic cords with free movement in the posterior vitreous cavity, centrally anchored to the optic nerve by a rod (usually anchored laterally in the ora serrata). Diagnosis: pars planitis (intermediate uveitis) and retinal detachment.	History of ocular injection given 1 month before	Point-of-care ultrasound showed fine hyperechoic cords in the left eye with free movement in the posterior vitreous cavity, centrally anchored to the optic nerve by a rod.	Patient diagnosed with pars planitis (intermediate uveitis) and detachment of the retina.
Yang et al	A total of 293 patients were evaluated, with anterior scleritis identified in 243 (327 eyes), posterior scleritis in 42 (57 eyes), and panescleritis in 8 (12 eyes). Anterior uveitis in 94 eyes (23.7%). B-mode ultrasound brought several findings to support the diagnosis and aid in the classification of scleritis, including posterior wall thickening and presence of fluid below Tenon's capsule, diagnosing posterior scleritis and panescleritis. The T sign (fluid inside the Tenon's capsule and in the optic nerve sheath) can be observed in the ultrasound evaluation.	Systemic and local diseases were evaluated in 39 patients (13.3%). Autoimmune diseases in 11.6% (34), rheumatoid arthritis in 13, ankylosing spondylitis in 10, gout in 4, relapsing polyarthritis in 4, and inflammatory bowel disease in 2. Infectious diseases in 2% (6). Five patients with a history of pulmonary tuberculosis were diagnosed and treated. Inactive leprosy in 1 patient. Granulomatosis with polyangiitis in 1 patient. Inflammatory pseudotumor in 2. Higher frequency of involvement by systemic and local diseases in panescleritis ( $P = .001$ ), especially tuberculosis ( $P = .009$ ).	The imaging findings acquired by B-mode ultrasound were vitreous opacity, posterior wall thickening, fluid below Tenon's capsule, and retinal and choroidal detachment.	Out of the 327 eyes evaluated with anterior scleritis, 35 exhibited vitreous opacity and 1 experienced retinal detachment. Of the 57 eyes with posterior scleritis, 57 presented with posterior wall thickening, 19 had fluid below Tenon's capsule, 5 had vitreous opacity, 3 experienced retinal detachment, and 1 experienced choroidal detachment. Of the 12 eyes with panescleritis, 12 had posterior wall thickening, 8 had vitreous opacity, 3 had fluid below Tenon's capsule, and 1 experienced choroidal detachment.
Cordero-Corna et al	The 4 cases exhibited normal ultrasound and T signal was absent. Diagnosis: posterior scleritis, performed by funduscopy or magnetic resonance imaging.	Not applicable.	—	—

**Table 3.** Quality of Evidence with the Use of Ultrasonography Assessment

Outcome	Quality of Evidence (GRADE <sup>24</sup> ) Range from +++++ to -----	Number of Participants (Studies Total Number)	Relative Effect (95% CI)	Comments
Use of B-scan ultrasound for anterior uveitis assessment	+ - - - - Very low	94 participants (1 study) <sup>16</sup>	—	Weak study methodology. Unable to verify the following factors: inconsistency, imprecision, and indirectness.
Use of B-scan ultrasound for intermediate uveitis assessment	+ - - - - Very low	47 participants (1 study) <sup>10</sup>	—	Weak study methodology. Unable to verify the following factors: inconsistency, imprecision, and indirectness.
Use of ultrasonography for ocular complications assessment	+ - - - - Very low	374 participants (2 studies) <sup>10,16</sup>	—	Weak study methodology. Unable to verify the following factors: inconsistency, imprecision, and indirectness.

which could be identified in 5 articles among those selected.<sup>10,13,14,16,22</sup>

Morphological changes such as the presence of punctate echogenicities in the vitreous humor<sup>4,5,9,10,12,16,23</sup> and thickening of the choroid or posterior wall<sup>8,10,12,16,22</sup> seem to be important parameters to be analyzed for the diagnosis of uveitis, as well as association with inflammatory joint diseases, requiring further studies with the B-mode. It is up to the examiner to identify the pathological entities present through a systematic analysis of the ocular structures, which appears to include static and dynamic evaluation using the transpalpebral technique, an important amount of conductive gel and care in order to avoid collapse the structures.<sup>3,4,5,10,14,19</sup> The use of a high-frequency transducer (ranging in the studies reported from 7.5 to 20 MHz)<sup>1,3,4,5,10,19,20,21</sup> seems to be the most suitable for better visualization and morphological analysis of the structures, and the variables must be adjusted during the evaluation.<sup>19</sup>

The diagnosis of uveitis by ultrasound could benefit patients with psoriatic arthritis, spondyloarthritis, and with inflammatory activity that does not improve with treatment, but there is still a lack of studies in the literature with a larger sample of patients that assess this end, which was found only in clinical cases isolated in this extensive review.

B-mode ultrasonography, in addition to evaluating joints, could complement your

investigation in the eyes, being a fast, dynamic, non-invasive, and low-cost tool to evaluate changes in vitreous humor, adding value in relation to other diagnostic methods, but there is still a need to be validated in inflammatory arthroplasties.

This review has the following limitations: the impossibility of comparative data analysis between studies due to the scarcity of papers; a statistical analysis of the association of uveitis with inflammatory joint diseases; impossibility of reproducing this imaging method for the evaluation of ocular alterations due to the absence of a detailed description of the ultrasound equipment specifications and of the technique used; as well as the difficulty in evidencing the effectiveness and accuracy of this imaging method due to the small size of the sample number and non-randomized and non-controlled studies.

### Conclusion

Vitreous opacity was one of the main parameters described, which represents an indication for the use of high resolution B-mode ultrasound for better visualization of the posterior chamber. Apparently, there are conflicting results regarding the reliability of the ultrasound evaluation as the main method of evaluation and not as a complementary technique to other diagnostic tests. In the literature, studies focused on ocular ultrasound findings in inflammatory arthropathies such as spondyloarthritis and psoriatic arthritis are not available, since the uveitis findings described,

specifically vitritis, are only reported in clinical cases. Further studies are needed in order to determine the diagnostic value of this technique, which is widely accessible, inexpensive, has very few contraindications, and offers minimal risk exposure to the patient.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – J.A.M.; Design – J.A.M.; Supervision – J.A.M.; Funding – N/A; Materials – R.de.F.T.C., I.C.R.; Data Collection and/or Processing – R.de.F.T.C., I.S.de.A.A.; Analysis and/or Interpretation – J.A.M., R.de.F.T.C.; Literature Review – J.A.M., R.de.F.T.C., C.C.C.; Writing – J.A.M., R.de.F.T.C.; Critical Review – J.A.M., R.de.F.T.C., C.C.C.

**Declaration of Interests:** The authors have no conflicts of interest to declare.

**Funding:** The authors declare that this study had received no financial support.

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