Original Article

B-Scan Ultrasonography Findings in Unilateral Posterior Scleritis

Arash Maleki[1,2], Maria Ruggeri[1,2], Amanda Colombo[1,2], Soheila Asgari[1,2], Sydney Look-Why[1,2], Shimy Apoorva[1,2], C. Stephen Foster[1,2,3]

[1]Massachusetts Eye Research and Surgery Institution, Waltham, MA, USA, [2]The Ocular Immunology and Uveitis Foundation, Waltham, MA, USA, [3]Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

Abstract

Purpose: To evaluate the B-scan ultrasound findings in unilateral posterior scleritis.

Methods: This was a retrospective observational case series at a tertiary uveitis clinic. The study population included patients who had been diagnosed with milder forms of unilateral posterior scleritis since 2010 and had B-scan ultrasonography of that eye. The healthy eye of each patient was considered the control eye for that patient.

Results: The average age of patients was 50.2 ± 17.8 (range, 18–67). Posterior scleritis was idiopathic in 6 (66.7%) patients and associated with rheumatoid arthritis in two and HLA-B27 ankylosing spondylitis in one patient. The thickness of the thickest area in the diseased eye was 2.08 ± 0.49 (range, 1.35–3.2) and the control eye was 1.53 ± 0.38 (range, 1.03–2.3). The difference between the symptomatic and control eye was statistically significantly different ($P = 0.02$). 1.7 mm was the cut-off-point on the receiver operating characteristics curve with the highest combined sensitivity and specificity of 87.5% and 88.9%, respectively. Comparing the thickness of the thickest section of the symptomatic eye of one patient with the same section in the other eye of the same patient, there was a difference of 20% or more in sclero-choroidal complex.

Conclusions: In this study, the sclero-choroidal complex thickness higher than 1.7 mm has the highest combined sensitivity and specificity. Comparing the thickest section of the symptomatic eye of one patient with the same section in the other eye can be diagnostic.

Keywords: B-scan ultrasonography, Posterior scleritis, Scleral nodule, Sclero-choridal complex, T-sign, Ultrasound

Address for correspondence: C. Stephen Foster, Massachusetts Eye Research and Surgery Institution, 1440 Main St. Ste. 201, Waltham, MA, USA.
E-mail: sfoster@mersi.com
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Introduction

Posterior scleritis is the painful inflammation of the sclera posterior to the equator. It is a less common and under-diagnosed type of scleral inflammation. Posterior scleritis can be seen across all age groups, although it most commonly affects middle-aged women.[1] The clinical features of posterior scleritis vary and can be mistaken with other entities such as orbital or intraocular inflammation and tumors.[2] Patients with full-blown posterior scleritis can present with periocular pain, vision loss, choroidal folds, disc edema, and exudative retinal detachment.[3] However, in milder forms of posterior scleritis, these signs might not be present, and these patients can be misdiagnosed with other diseases, especially neurological issues.

The mainstay of diagnosis of posterior scleritis is B-scan ultrasonography. The range of ultrasonographic abnormalities in patients with posterior scleritis includes thickening of ocular coats, fluid in the episcleral space, enlargement of the optic nerve shadow, and subretinal fluid.[3] "T-sign", the fluid accumulation between the optic nerve and the sclera, is the pathognomonic sign for posterior scleritis.[4] Based on the previous studies, the normal scleral thickness ranges between 0.5 and 2.0 mm with a thickness of over 2.5 mm as

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a criterion for the diagnosis of posterior scleritis.[3,4] B-scan ultrasonography findings have been shown to be reproducible in an expert hand.[4]

It has been hypothesized that sclero-choroidal thickness values <2.0 mm can be indicative of inflammation in a symptomatic patient;[4] however, this concept has not been completely studied. In this current study, we evaluated the B-scan ultrasound findings in milder forms of unilateral posterior scleritis, which had either not been diagnosed or had been misdiagnosed as nonocular problems.

Methods

This was a retrospective observational case series at a tertiary uveitis clinic. This study was approved by the New England Institutional Review Board for chart review, was conducted in accordance with the Declaration of Helsinki and was Health Insurance Portability and Accountability Act compliant.

The study population included patients who had been diagnosed with unilateral posterior scleritis since 2010 and had standard B-scan ultrasonography of that eye. Those patients with hyperopia more than +3.0 and myopia more than −3.0 diopters were excluded from the study. Patients with ocular issues such as choroidal effusion syndrome and systemic diseases such as thyroid ophthalmopathy, which might affect the sclero-choroidal complex thickness or may mimic posterior scleritis, were excluded from the study. We excluded patients with anterior scleritis to study isolated cases of posterior scleritis. We also excluded patients with full-blown posterior scleritis in the clinical examination; thus, we were able to study characteristics of the milder forms of posterior scleritis. These clinical signs included choroidal folds, serous macular or retinal detachment, and disc edema.

Systemic rheumatologic conditions associated with posterior scleritis, demographic data, clinical data, therapeutic data, and their duration were collected from the patients' electronic charts. This data included age, gender, race, and eye affected by scleritis. Extensive blood work-up had been done for all infectious and noninfectious causes of posterior scleritis. Fluorescein angiography, Humphrey visual field, as well as brain and orbital magnetic resonance imaging with and without contrast had been done in patients who were suspicious for intraocular inflammatory diseases, optic neuritis, and orbital inflammatory syndromes, respectively.

B-scan ultrasonography (Accutome® Inc., Malvern, PA, USA) was conducted by experienced technicians. B-scan ultrasonography protocol included five sections: 12T (transverse), 9T, 6T, 3T, and axial horizontal from both eyes. The video for each section was observed by two of the authors (A.M. and C.S.F.), and the most consistent images of posterior sclero-choroidal thickness in each section were chosen for the sclero-choroidal complex thickness measurement and statistical analysis**.** The thickest line between two corresponding points for each cut, both the thickest and the thinnest sections [Figure 1a-c], and the average of five selected images were measured or calculated. All measurements were confirmed by the senior author (C.S.F.). For thickness measurement in B-scan, calipers in the measurement window of B-scan machine software were used to measure the distance between the first spike at the back of the eye (retina) and the outer part of the sclera excluding the areas with episcleral fluid.

Active disease was defined as a symptomatic eye with gross thickening of one or more sections on B-scan in comparison to other sections of that eye (regardless of the actual thickness), episcleral fluid, enlargement of optic nerve head, typical T-sign, or a combination of these signs. Each study eye had at least one of these signs on B-scan. A response to experimental immunosuppressive therapy for scleritis, both clinically and on B-scan, was also considered active scleritis. Remission was defined as resolution of symptoms and improvement or the resolution of B-scan ultrasonography findings.

The primary outcome was to find a more sensitive criteria in patients with possible posterior scleritis. The secondary outcomes were if the sclero-choroidal thickness in the thickest area in the affected eye was significantly thicker than that of the control eye in each patient, and comparing the average thickness of both the thickest and thinnest areas between the affected eye and the control eye.

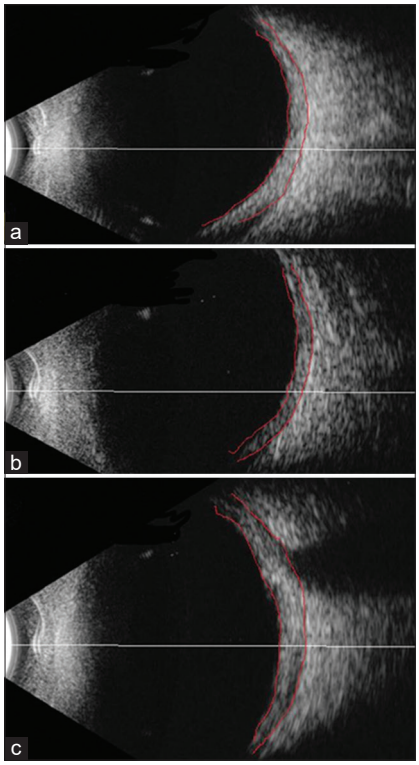

Figure 1: Marking the anterior and posterior borders of sclero-choroidal complex thickness in different sections of one of the study eyes. Measurements were done for the thickest area of each section. (a) Transverse 12 o'clock, (b) Transverse 9 o'clock (thinnest section), and (c) Axial horizontal (thickest section)

Statistical analysis

Statistical analysis was performed using Med Calc Statistical Software: Release 19.3 (Med Calc Ltd, Acacialaan, Ostend, Belgium). Categorical variables were described as counts and percentages, and continuous variables were described as means and standard deviation. We used generalized estimating equation (GEE) to compare the thickest, thinnest, and average sclero-choroidal thickness between the affected and control eyes of each patient and to consider the correlation between two eyes of each patient. The receiver operating characteristics (ROC) curve was used to find the sclero-choroidal complex thickness which can differentiate between affected and control eyes of each patient with high sensitivity and specificity. $P \leq 0.05$ was considered statistically significant.

Results

Nine patients with unilateral posterior scleritis (9 eyes) were included in this study. The asymptomatic eye of each patient was used as a control eye for that patient.

The average age of patients was 50.2 ± 17.8 (range, 18–67). Female to male ratio was 6/3 (66.7%). The right eye was affected in 5 (55.5%) patients.

Posterior scleritis was idiopathic in 6 (66.7%) patients. It was associated with rheumatoid arthritis in 2 (22.2%) and HLA-B27 ankylosing spondylitis in 1 (11.1%) patients. In regard to clinical manifestations, pressure-like pain was present in 4 (44.5%) patients, tenderness in three patients (33.4%), blurry vision in two patients (22.2%), as well as irritation and light sensitivity each in one (11.1%) patient. Ocular examination was normal in all eyes, except for painful eye movements with no restrictions. Prednisone had been started after diagnosis in 4 (44.5%) patients. One of the patients with idiopathic posterior scleritis responded to initial dosing of prednisone and was thus not subsequently started on immunomodulatory therapy (IMT). Medications employed included: Naproxen in 3 (33.3%) patients, azathioprine in 3 (33.3%) patients, celexocib 2 (22.2%), methotrexate, tocilizumab, adalimumab, infliximab, mycophenolate mofetil, and rituximab each in 1 (12.2%) patient. Six (66.7%) patients achieved remission. Successful treatment regimens included: Methotrexate in 1 (12.2%) patient, azathioprine in 1 (12.2%) patient, rituximab in 1 (12.2%) patient, combination of adalimumab and mycophenolate mofetil in 1 (12.2%) patient, and combination of infliximab and azathioprine in 1 (12.2%) patient [Table 1].

The thickest area varied from patient to patient. It was 12T in 4 (44.4%) patients (eyes), axial horizontal in 2 (22.2%) patients (eyes), and 1 (11.1%) patient (eye) in 9T, 6T, and 3T views. The thickness of the thickest area in the diseased eye was 2.08 ± 0.49 (range, 1.35–3.2), and the control eye was 1.53 ± 0.38 (range, 1.03–2.3). The thickness of the thinnest area in the diseased eye was 1.23 ± 0.21 (range, 1.03–1.59), and the control eye was 1.31 ± 0.16 (range, 0.97–1.48). The average thickness of all sections in the diseased eye was 1.43 ± 0.32, and the control eye was 1.23 ± 0.28 [Table 2]. Using GEE for the thickest sections, thinnest sections, and the average of all sections, the thickness difference between the symptomatic and control eye was statistically significantly different for the thickest sections ($P = 0.002$) and the average of all sections ($P = 0.003$). The thinnest sections between the symptomatic and control eyes were not statistically different ($P = 0.19$).

Four of the studied eyes had two sets of B-scan ultrasonography. One of them achieved remission on successful IMT, resulting in the thickest area decreased from 2.3 mm to 1.42 mm. The following three patients did not achieve remission on IMT and changes in sclero-choroidal complex thickness did not decrease except in one patient with resulting sclero-choroidal complex thickness decrease from 2.06 mm to 1.45 mm, yet still symptomatic. One patient had three sets of B-scan ultrasound [Figure 2]. The second set was taken when the disease was active, and there was no significant change in the thickness of the thickest area, 2.3 mm to 2.16 mm; however, after remission on rituximab therapy, the change of the thickest area decreased significantly from 2.16 mm to 1.50 mm between the 2nd and 3rd sets of B-scan ultrasonography. In the control

Table 1: Patients' demographics

Patient number	Age	Gender	Systemic rheumatologic disease
Patient 1	18	Male	None
Patient 2	67	Male	Rheumatoid arthritis
Patient 3	64	Female	Rheumatoid arthritis
Patient 4	64	Female	HLA-B27 ankylosing spondylitis
Patient 5	61	Female	None
Patient 6	36	Male	None
Patient 7	65	Female	None
Patient 8	42	Female	None
Patient 9	35	Female	None

HLA: Human leukocyte antigen

Table 2: B-scan ultrasonography findings other than thickening and successful treatment

Patient number	Eye involved	Other findings (OD)	Other findings (OS)	Successful treatment
Patient 1	OS	None	None	None
Patient 2	OD	None	None	MTX
Patient 3	OS	None	None	AZA
Patient 4	OS	None	Fluid 3T and 12T	RIT
Patient 5	OS	None	Fluid 9T	None
Patient 6	OD	Fluid 12T and 6T	None	None
Patient 7	OD	None	None	Oral pred
Patient 8	OD	Fluid 9T and T-sign	None	MMF and ADA
Patient 9	OD	ON enlargement	None	INF and AZA

ADA: Adalimumab, AZA: Azathioprine, INF: Infliximab, MMF: Mycophenolate mofetil, MTX: Methotrexate, OD: Right eye, ON: Optic nerve, OS: Left eye, Pred: Prednisone, RIT: Rituximab, T: Transverse

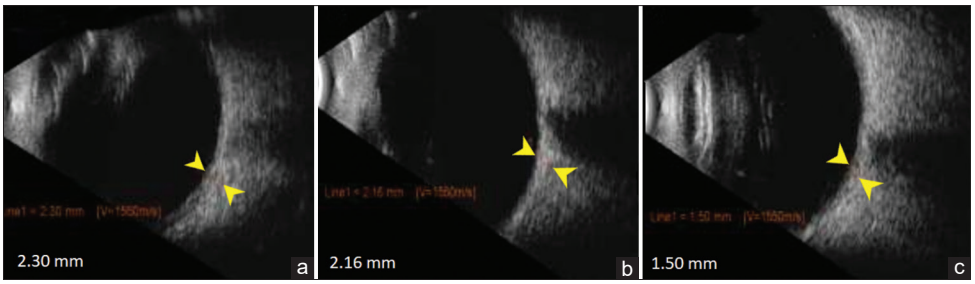

Figure 2: (a) Thickening of the sclero-choroidal complex (2.30 mm) before starting treatment in axial horizontal section (b) The same section 2 months after unsuccessful treatment (2.16 mm) (c) The same sections 3 months after successful treatment (1.50 mm)

eyes of these four patients, the changes in the thickness of the thickest area were not statistically significant. The average difference in percentage between the study and the control eyes in each patient were 28% ± 3.7% (range, 18%–56%), [Table 3].

Four patients in the disease group had episcleral fluid in one or more areas, all associated with the thickest area [44.5%, Figure 3]. Furthermore, one patient had a scleral nodule [11.1%, Figure 4] one had typical T-sign (11.1%) which was associated with the thickest area, [Figure 5] and one with optic nerve head enlargement [11.1%, Figure 6].

Using ROC-curve, we found that the ideal thickness for considering it as posterior scleritis with 87.5% sensitivity and 88.9% specificity is 1.7 mm [ideal point on the curve with highest combined sensitivity and specificity, Figure 7].

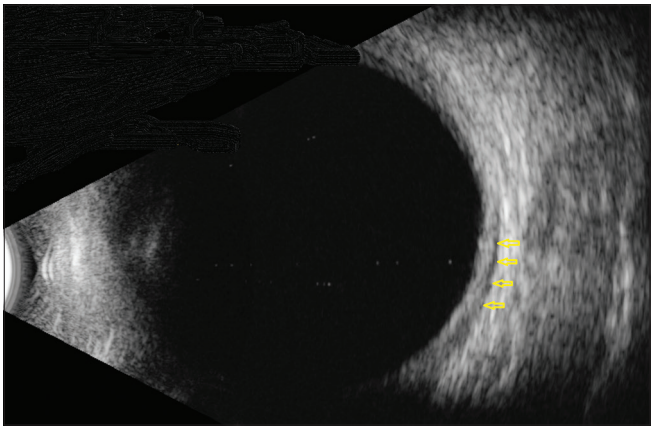

Figure 3: The presence of fluid accumulation in supra-scleral space (yellow arrows)

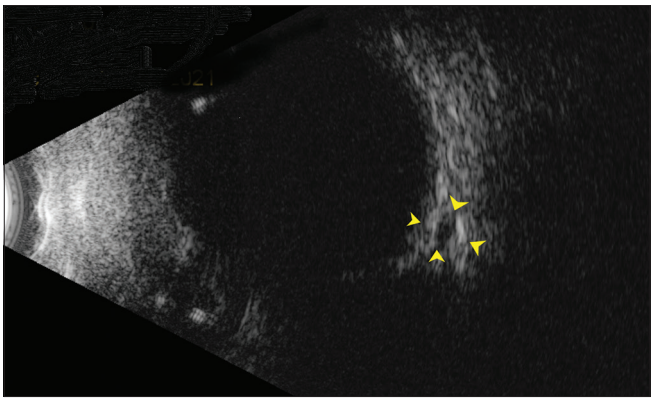

Figure 4: The scleral nodule and fluid accumulation (defined by markers)

Discussion

Posterior scleritis accounts for 2%–12% of all cases of scleritis in the literature.[5] Its association with systemic diseases has been found to be significantly lower than other types of scleritis;[5] however, it can progress to become a vision-threatening condition.[3] Early diagnosis and aggressive therapy might be indicated to prevent sight-threatening complications. For early diagnosis, a reliable and sensitive diagnostic test and criteria are crucial.

Although B-scan ultrasonography is the gold standard diagnostic test for posterior scleritis, the standard protocols and the necessary views have not been described in the limited body of literature. Moreover, in the normal population, the sclero-choroidal complex thickness has a wide range between 0.5 mm and 2.0 mm.[3] With considering this wide range, people with thinner sclera can be missed with B-scan ultrasonography, and patients with thicker sclera can be falsely over-diagnosed based on these strict diagnostic criteria. In other words, many patients with thinner sclero-choroidal complex can be inflamed with <2 mm thickness.

Most posterior scleritis studies have focused on epidemiology, diagnosis, and treatment. In almost all studies, a thickness of more than 2.5 mm has been considered a criterion for the diagnosis of posterior scleritis.[3,4] Additionally, in some studies, it has been mentioned that patients with posterior scleritis can be asymptomatic.[3,4] We believe that these discrepancies are caused by a strict thickness criterion in B-scan sonography for patients with posterior scleritis.

Although the current diagnostic criteria seem to be specific, it may not be sensitive enough, and some patients with a milder form of posterior scleritis are overlooked with the current thickness criteria. The sclero-choroidal complex thickness in most of our patients were <2.0 mm, yet they responded to therapy clinically, and two patients with two or three sets of B-scan ultrasonography showed significant improvement in the thickest area of the sclero-choroidal complex thickness.

The aim of this study was to find a more sensitive criteria in patients with milder or possible posterior scleritis based on

Table 3: Sclero-choroidal thickness in all views (study eye versus control eye)

Patient number	Eye	Laterality	12T (mm)	9T (mm)	6T (mm)	3T (mm)	Ax-Hor (mm)	Difference[1,2,3,4] (%)
Patient 1	Study eye	OS	1.99	1.23	1.23	1.77	1.64	20
	Control eye	OD	1.58	1.48	1.23	0.97	1.38	
Patient 2	Study eye	OD	1.49	1.56	1.78	1.55	1.63	32
	Control eye	OS	1.36	1.44	1.22	1.01	1.41	
Patient 3	Study eye	OS	1.03	1.21	0.97	1.35	1.22	24
	Control eye	OD	0.97	0.79	0.48	1.03	1.11	
Patient 4	Study eye	OS	1.45	1.22	1.3	1.31	2.3	40
	Control eye	OD	1.04	1.39	1.39	1.46	1.38	
Patient 5	Study eye	OS	2.06	0.98	0.97	1.46	1.7	18
	Control eye	OD	1.7	1.31	1.34	1.1	1.76	
Patient 6	Study eye	OD	1.59	1.63	1.21	1.21	1.94	16
	Control eye	OS	2.1	1.15	1.83	1.3	1.64	
Patient 7	Study eye	OD	2.01	2.05	1.69	1.38	1.7	20
	Control eye	OS	1.77	1.65	1.59	1.82	1.55	
Patient 8	Study eye	OD	3.2	2.35	1.95	1.03	2.19	28
	Control eye	OS	1.41	1.37	1.77	1.91	1.67	
Patient 9	Study eye	OD	2.09	1.59	1.76	1.78	1.82	N/A
	Control eye	OS	N/A	N/A	N/A	N/A	N/A	

[1]Difference between the thickest area in the study eye and the same area in the control eye for each patient in percent, [2]The difference of the thickest area between the symptomatic and control eye was statistically significantly different (P=0.02), [3]The difference of the thinnest area between the symptomatic and control eyes was not statistically different (P=0.3), [4]The difference in the average thickness between the symptomatic and control eyes was not statistically different (P=0.34). Ax-Hor: Axial horizontal, N/A: Not available, OD: Right eye, OS: Left eye

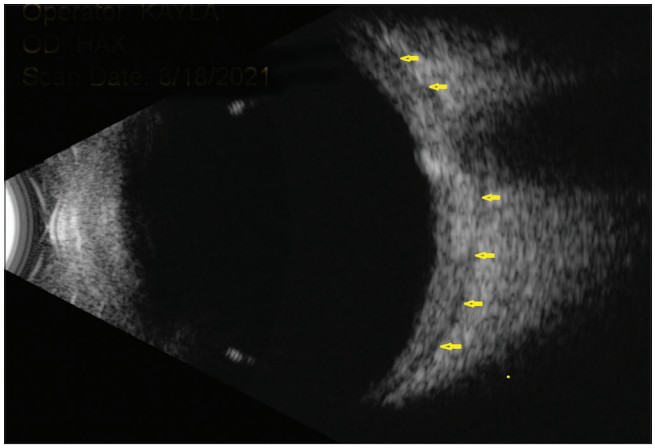

Figure 5: The typical T-sign in axial horizontal view (marked by arrows)

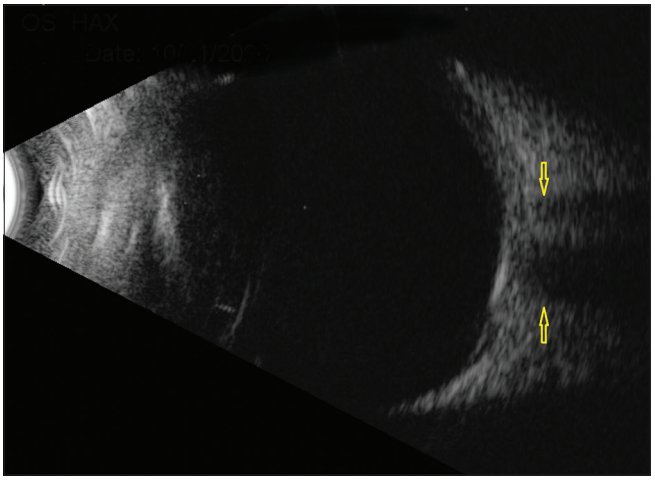

Figure 6: Optic nerve head enlargement demarcated by arrows

comparing the symptomatic eye diagnosed with posterior scleritis in one patient to the contralateral eye of the same patient, deemed as the control eye. We decided to study unilateral posterior scleritis patients so that we could avoid selection bias by using a different control group in a tertiary uveitis clinic considering the wide range of scleral thickness in the normal population.

The concept of sclero-choroidal complex thinner than 2 mm in posterior scleritis was previously considered by Suhr and Patel.[4] They measured the mean cross-section of the sclera at the posterior pole and used that measurement for statistical analysis. They compared the measurements with a control group. Based on their results, it is not clear how many unilateral and how many bilateral cases were included in their study. In their unilateral cases, they used the patients' other eyes as control eyes; however, the number of these patients has not been mentioned. Their study was prone to selection bias because of these flaws.

Our results clarified the confusions of the Suhr and Patel study. The thickness measurement of the most thickened section in our patients was lower than that of the Suhr and Patel study. This result may be from the earlier stages or milder forms of the disease in our patients, or from different methods of measurement as they did not clarify how they measured the thickness. As described in the "Methods" section, the thickness measurements within our study were done with careful selection of the thickest measurement in each view, which was done by watching the video of B-scan ultrasound obtained for each section based on B-scan ultrasonography machine setting.

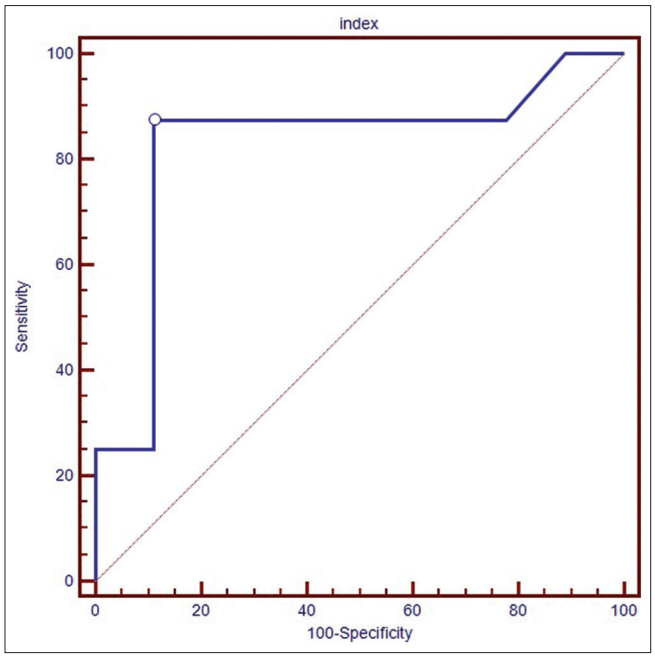

Figure 7: Receiver operating characteristics curve demonstrated that the ideal thickness for considering it as posterior scleritis with 87.5% sensitivity and 88.9% specificity is 1.7 mm (ideal point on the curve with highest sensitivity and specificity)

Comparing the thickest area of the study eye and the control eye, we found that the average and minimal difference in percentage between two eyes were 28% and 20%, respectively. This means that the difference in the thickest area between two eyes should be at least 20% to be considered as thickened sclera and subsequently posterior scleritis. This criterion is important in milder forms of unilateral posterior scleritis when the other criterion is not met (thickness ≥1.7 mm).

Interestingly, we also found that the posterior scleritis can be localized even with no nodule that can be seen in nodular scleritis since the thickest section varied from one patient to another. Additionally, the thickest area was not always the posterior pole. Based on this observation, we recommend obtaining B-scan sonography from superior, inferior, nasal, temporal, and axial horizontal while considering the thickest section and the thickest area of each section for the diagnosis of posterior scleritis. Moreover, comparing the thickness of the thickest area in the symptomatic eye with the same view of the contralateral eye can be especially informative in unilateral cases; however, these theories should be examined with a more potent study.

The significant decrease in the sclero-choroidal complex thickness in the thickest area with no changes in the thinnest and the average of all views may indicate the reliability of B-scan sonography in the follow-up of the patients with posterior scleritis.

Using the ROC curve, we found a new cut-off-point (1.7 mm) with higher combined sensitivity and specificity in patients with posterior scleritis. This new cut-off-point may be more sensitive and could help diagnose patients with milder forms of the disease and even posterior scleritis patients at an earlier stage, avoiding the later stages which can be vision threatening. The new cut-off-point showed a sensitivity of 87.5% and specificity of 88.9%. Although an ideal cut-off-point should depict 100% sensitivity and specificity, this does not typically occur in a clinical setting. A good and realistic cut-off-point is a sensitivity and a specificity between 80% and 90%.[6] The new cut-off-point has good to excellent sensitivity and specificity; however, based on the small study population, this cut-off-point should be examined in more potent studies with a larger patient population.

We might be criticized for using the ROC curve for a small study population. We admit that the small sample size may affect the power of the study. However, we should note that the incidence and prevalence of scleritis are 3.4 and 5.2 per 100,000 patient-year, respectively,[7] and posterior scleritis includes a small percentage of all patients with scleritis (2%–12%).[5] This means that the incidence of posterior scleritis is between 0.06 and 0.3 per 100,000 patient-year. Since posterior scleritis is considered a rare disease based on these calculations, it is reasonable to use a ROC curve to calculate a new cut-off-point for a gold standard diagnostic tool in our study. We should also consider that most of these patients had not been diagnosed or had been misdiagnosed with a nonocular disease. This implies that the current B-scan criteria for posterior scleritis are not sensitive enough, at least for milder forms or earlier stages of the disease. Additionally, the purpose of ROC curve in this study was not defining the specificity and sensitivity of B-scan, since B-scan is the gold standard test for posterior scleritis. The purpose of using ROC curve in this study was to find the highest combined sensitivity and specificity. The normal shape of the ROC curve and the compatibility of ROC curve results with *t*-tests which showed significant differences are the other supportive information for this study.

Based on these findings, we hypothesize a new criteria for the diagnosis of posterior scleritis. The criteria include a scleral thickness higher than 1.7 mm in a symptomatic eye. This number can be helpful in bilateral posterior scleritis. The second criterion which can be used especially in unilateral cases is to compare the thickest area in the symptomatic eye with the same area in the control eye. This criterion is also applied to a symptomatic eye. It is important to consider that the same areas of both eyes should be compared with each other. Additionally, this comparison should be done on anatomical areas, not based on the clock hour. This is important for horizontal transverse views. This means that transverse 9T of the right eye is comparable with transverse 3T of the left eye (both temporal views) and transverse 3T of the right eye is comparable with transverse 9T of the left eye (both nasal views). It is important to note either criterion is sufficient for the diagnosis of posterior scleritis when it is met.

There are some limitations for this study, most of them secondary to the retrospective nature of the study. Small sample

size was another major drawback of this study; however, we should consider that posterior disease is a rare entity and mostly undiagnosed. We also had strict exclusion and inclusion criteria to control the confounding factors and to avoid selection bias toward extreme and full-blown cases. This was another cause of the small study population. Some patients did not have another B-scan ultrasonography during their follow-up period when they achieved remission, making it so that we were unable to comment on the role of ultrasound in all of our patients.

In conclusion, we introduced a new criteria for the diagnosis of posterior scleritis, especially in milder forms. First, the sclero-choroidal complex thickness higher than 1.7 mm. Second, a difference of 20% or more in sclero-choroidal complex thickness between the symptomatic eye of one patient with the same section in the other eye of that patient. One criterion is sufficient for the diagnosis of posterior scleritis when it is met. However, these findings should be evaluated with more potent studies with a larger sample size.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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