· Clinical Research ·

Evaluation of retina and choroid *via* OCT in anti-DFS70/ LEDGF positive healthy individuals

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Abstract
● **AIM:** To investigate the association between anti-DFS70 antibody positivity and ocular parameters, specifically, the choroidal vascularity index (CVI) and other optical coherence tomography (OCT) metrics, in a healthy population.
● **METHODS:** This age- and sex-matched case-control study enrolled 84 healthy individuals with positive anti-DFS70 antibody findings and 84 healthy negative controls. All participants underwent detailed ophthalmological examinations, including biometry and OCT imaging. Anti-DFS70 positivity was determined by indirect immunofluorescence and scored semi-quantitatively (1+ to 3+). CVI was calculated from OCT images using a standardized protocol with Image J software. Statistical analyses, including Student's *t*-test, Mann-Whitney *U* test, Spearman correlation, and logistic regression, were used to compare groups and identify predictive factors.
● **RESULTS:** The individuals who tested positive and negative for anti-DFS70 included in the study were matched for age (median age=47y) and sex (F:M=7:1). CVI was significantly lower in the anti-DFS70-positive group compared to the negative group. A higher anti-DFS70 antibody titer was significantly associated with decreased subfoveal and nasal choroidal thickness (P=0.016 and P=0.014, respectively). In univariate regression analysis, CVI was the only significant predictor of anti-DFS70 positivity [odds ratio (OR)=0.02, P=0.025]. Multivariate analysis revealed a positive correlation between macular thinning outside the subfoveal area and anti-DFS70 status (P<0.05).
● **CONCLUSION:** Our study demonstrates a novel association between anti-DFS70 antibody positivity and reduced choroidal vascularity in healthy individuals. These findings suggest that anti-DFS70 antibodies may be associated with subtle choroidal vascular changes detectable by OCT, even in asymptomatic individuals. Further longitudinal research is warranted to clarify the underlying mechanisms and long-term clinical significance of these ocular changes.
● **KEYWORDS:** anti-DFS70 antibodies; choroidal vascularity index; optical coherence tomography; autoimmunity
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INTRODUCTION
Anti-DFS70 antibodies, also known as antibodies targeting the lens epithelium-derived growth factor (LEDGF), represent a significant focus of research in the field of autoimmunology. The term "DFS70" originally referred to the staining pattern observed in indirect immunofluorescence (IIF) assays, and studies have confirmed that the underlying antigen is indeed LEDGF, a nuclear protein involved in transcriptional regulation[1]. These antibodies have been identified as potential indicators of systemic autoimmune rheumatic diseases (SARD) but are also prevalent in healthy individuals, necessitating a nuanced understanding of their clinical implications.

The detection of anti-DFS70 antibodies is particularly relevant because their presence is often associated with both autoimmune and non-autoimmune conditions. Studies have shown that while anti-DFS70 antibodies can be found in patients with SARD, such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and undifferentiated connective tissue disease (UCTD), they are more commonly observed in healthy populations or those with other non-SARD conditions, such as fibromyalgia and atopic diseases[2-3]. Specific findings indicate that high-titer anti-DFS70 antibodies correlate with non-SARD conditions, supporting the hypothesis that these antibodies may not only be indicative of autoimmune processes but could also possess protective qualities in specific contexts[2,4]. This dual nature complicates their interpretation in clinical practice, as positive results do not automatically signify a specific autoimmune diagnosis[4].

The prevalence of anti-DFS70 antibodies varies significantly across different populations. In healthy individuals, reports have suggested a prevalence rate of approximately 5%-10%[2,5]. For instance, a multicenter study reported a positive rate of around 21.29% among healthy subjects screened for autoantibodies[6]. In contrast, among patients with SARD, the rate of isolated anti-DFS70 positivity has been cited as less than 1%, indicating that these antibodies are far more common in the general population than in those with systemic autoimmune conditions[7]. Furthermore, studies observing cohorts with UCTD found a higher prevalence of anti-DFS70 antibodies up to 13%, demonstrating that while these antibodies may rarely signal SARD, they can be found in non-progressing chronic inflammatory states[8].

Historically, the understanding of anti-DFS70 antibodies has evolved over the past two decades. Since their initial identification, considerable research has focused on the correlation between anti-DFS70 positivity and various clinical conditions[9]. While earlier studies primarily associated anti-DFS70 with SLE and other autoimmune diseases, recent findings illustrate a trend towards recognizing their presence as more benign and even protective in specific populations, reflecting a significant shift in understanding their clinical utility over time[10]. Modern analyses emphasize incorporating these antibodies in routine diagnostic panels to enhance the specificity of autoimmune disease diagnoses, thus reducing unnecessary follow-ups for patients who present with isolated anti-DFS70 positivity[1,8,10].

The choroidal vascularity index (CVI) serves as a crucial biomarker for assessing the health and structure of the choroidal vasculature. Defined as the ratio of the luminal area to the total choroidal area, the CVI provides insight into both vascular and stromal elements of the choroid, making it a more reliable indicator of choroidal health than traditional measurements such as choroidal thickness (CT) alone[11-12]. This index is particularly significant as it has been associated with various ocular conditions, including diabetic retinopathy, uveitis, and age-related macular degeneration. Studies suggest that CVI can reflect changes in choroidal vascularity stemming from pathologies like diabetes, offering a non-invasive means of tracking disease progression[11,13].

Optical coherence tomography (OCT) parameters play a pivotal role in evaluating retinal health. OCT facilitates high-resolution imaging of retinal structures, allowing for meticulous examination of retinal layers and associated metrics such as retinal nerve fiber layer thickness, ganglion cell-inner plexiform layer thickness, and central macular thickness (CMT). These parameters are critical for diagnosing and monitoring common conditions like diabetic macular edema and glaucoma. The relevance of both CVI and OCT parameters in ocular health assessments cannot be overstated. These measures serve not only as diagnostic tools but also as prognostic indicators of disease outcomes. Studies have shown that certain OCT measurements are strongly correlated with visual function and disease severity in many age-related and oxidative damage-induced vascular and neurodegenerative diseases[14-15]. In this regard, studies conducted on rat eye specimens using IIF, anti-DFS70 antibodies showed intense reactivity against the reticular lens bands, the corneal layers, and the ciliary muscle[16]. Similarly, in studies conducted on rat models, treatment with LEDGF resulted in increased photoreceptor survival in retinas with photoreceptor damage[17]. Although LEDGF has been demonstrated to be more prevalent in the anterior segment structures of the cornea and lens, LEDGF has been shown to have the potential to mitigate the harmful effects of ultraviolet B (UVB) by reducing DNA strand breaks in retinal pigment epithelium (RPE) cells[18].

We recognize that oxidative stress and subsequent RPE damage are among the key pathophysiological mechanisms in all of these diseases where OCT is used for diagnosis and follow-up. Additionally, the potential protective effect of LEDGF in this context, which has been demonstrated in animal models, has not yet been evaluated using OCT parameters. This represents a significant gap in the literature.

PARTICIPANTS AND METHODS

Ethical Approval The study protocol was approved by the Ethics Committee of the Uşak University Faculty of Medicine (Approval number: 208-208-10). All procedures were performed in accordance with the ethical standards of the National Research Committee, the 2024 Helsinki Declaration and its later amendments, and comparable ethical standards. Written informed consent was obtained from all the participants.

Data Collection and Analysis Cases with positive anti-DFS70 findings in laboratory tests following rheumatological examinations between 2022 and 2024 were included in the ophthalmological evaluation. After detailed eye examinations and OCT scans, patients were placed under routine follow-up. Cases aged 18–65y with no rheumatological disease detected during a 1-year follow-up were included in the study. To ensure the statistical independence of data points and prevent biased variance estimates and inflated significance caused by inter-eye correlation, all analyses were conducted using data from the right eye of each participant. This unilateral method is a conventional strategy in ophthalmic research studying systemic conditions, where both eyes are affected equally by systemic factors and are therefore not independent observations. Exclusion criteria included a history of intraocular surgery within one year of antibody positivity, diagnosis of rheumatological disease, pre-existing retinal pathology, refractive error exceeding 3 diopters of hyperopia or myopia, and diagnosis of glaucoma. Additionally, the use of anticholinergic medications that could affect dry eye or retina-choroidal measurements and lens opacities that would hinder evaluation of the retina-choroidal interface were grounds for exclusion. Before imaging, comprehensive ophthalmological assessments were performed, including examinations of visual acuity, the anterior segment, intraocular pressure measured by applanation tonometry, and fundus evaluation. OCT measurements were obtained between 9:00 and 11:00 *a.m.*, following dilation for standardization. Imaging was performed using the Canon OCT-HS100 (Canon Inc., Tokyo, Japan) device and embedded software (v.4.5.3); since the device lacks an enhanced depth imaging module, images including the scleral border were manually captured for choroidal measurements. These images were exported in *.bmp* format, and CT was measured at three points with Image J v.1.54g (NIH, Bethesda, MD, USA) software. The CVI was calculated following the method described previously[18]. The process involved marking the choroidal area, converting images from RGB to 8-bit format, applying Niblack auto local thresholding, color thresholding, and calculating the ratio within the intersecting area as macros, aside from manual choroidal marking. Other parameters, including keratometry, central corneal thickness (CCT), white-to-white distance (WTW), anterior chamber depth (ACD), and axial length (AL), were measured using the Nidek AL-Scan (Nidek Co, Aichi, Japan) optical biometer. All right eye measurements of the cases were evaluated within the scope of the study. Antinuclear antibodies (ANA) profiling was performed using the IIF method with HEp-20-10 cells (Euroimmun FB 1512-1005-1, Lübeck, Germany). However, anti-DFS70 positivity was scored on a scale of 0–3 as either negative or 1+/2+/3+ instead of as a continuous variable.

Statistical Analysis The number of cases in the study was calculated a priori using G*Power (v3.1.9.7, Düsseldorf, Germany) with a two-tailed effect size of 0.6 and a power of 0.95, considering similar studies in the literature, and a minimum of 74 cases for each group was considered necessary. Considering potential negative factors related to the device and patients, a total of 100 cases were included in both groups, and those with image quality ratings below 8/10 and the choroidal assessment threshold were excluded. In this case-control study, 84 subjects were included in each group, matched for age and gender. SPSS 15.0 for Windows (IBM Corp., Armonk, NY, USA) software was used for statistical analysis. Descriptive statistics were presented as counts and percentages for categorical variables and mean, standard deviation, median, and interquartile range for numerical variables. Ratios between groups were compared using the Chi-square test. Comparisons of numerical variables between two independent groups were performed using the student *t*-test when the normal distribution condition was met, and the Mann-Whitney *U* test when it was not. Relationships between numerical variables were examined using Spearman correlation analysis since the parametric test condition was not met. Logistic regression analysis was performed to assess the effect of determining factors. The alpha significance level was set at $P<0.05$.

RESULTS

The individuals who tested positive and negative for anti-DFS70 included in the study were matched for age (median age=47y) and sex (F:M=7:1) and showed no significant difference in refraction ($P=0.145$). Anti-DFS70 positivity was distributed within the study group as follows: 14.2% (+), 22.6% (2+), and 63.1% (3+). The only significant difference observed in the measurements of the anterior segment and OCT parameters was in the CVI, which was higher in the Anti-DFS70-negative group (Table 1). Since the macular measurements in the inferior and temporal quadrants followed a normal distribution. Similarly, the choroidal measurements in the nasal and temporal quadrants also followed a normal distribution; the student's *t*-test was used to compare these measurements. In the correlation analysis, no statistically significant relationship was found between CVI and the measurements (all $P>0.05$). As the anti-DFS70 titer increased, a significant decrease was observed in the subfoveal and nasal choroidal thicknesses ($P=0.016$, $P=0.014$; Table 2). CVI was the only statistically significant predictor of anti-DFS70-positive status in the univariate model [odds ratio (OR)=0.02, $P=0.025$]. In the multivariate model, the superior, temporal, nasal, and inferior macular areas were positively associated and statistically significant (superior $P=0.021$, others $P<0.001$; Table 3).

DISCUSSION

In this case-control study, we examined retinal and choroidal structures using OCT in healthy individuals with anti-DFS70/LEDGF antibody positivity. Our main finding was a significantly lower CVI in anti-DFS70-positive subjects compared to controls, with no notable differences in demographic or other ocular parameters. Additionally, higher anti-DFS70 antibody titers correlated with reduced subfoveal and nasal CT.

An intriguing and complex finding was the lack of a significant correlation between CVI and anti-DFS70 antibody titer ($r=-0.133$, $P=0.230$), despite most cases showing strong (3+)

Table 1 Demographic characteristics and intergroup measurement comparisons

Parameters	Anti-DFS70		
	Positive	Negative	P
Age, median (IQR), y	47.0 (31.0-56.5)	47.0 (31.0-56.5)	1.000[a]
Sex (n), F/M	74/10	74/10	1.000[b]
Refraction, median (IQR), D	0.25 (-0.88-1.00)	-0.25 (-0.75-0.50)	0.145[a]
Intraocular pressure (mm Hg), median (IQR)	14 (12-19)	14 (11-19)	0.158[a]
Anti-DFS70, n (%)			
+	12 (14.2)		
++	19 (22.6)		
+++	53 (63.1)		
Axial length (mm), median (IQR)	23.4 (22.4-24.1)	23.4 (23.0-24.1)	0.614[a]
White-to-White distance (mm), median (IQR)	12.1 (11.8-12.3)	12.1 (11.9-12.4)	0.073[a]
Anterior chamber depth (mm), median (IQR)	3.4 (2.8-4.2)	3.3 (3.0-3.7)	0.512[a]
Central corneal thickness (μm), median (IQR)	535.0 (511.0-567.5)	541.0 (514.0-575.0)	0.557[a]
Macula (μm)			
Superior median (IQR)	314.0 (288.5-333.0)	308.0 (288.0-344.5)	0.731[a]
Inferior, mean±SD	301.5±32.2	293.0±38.1	0.119[c]
Temporal, mean±SD	297.2±32.1	305.4±39.1	0.140[c]
Nasal, median (IQR)	305.0 (276.0-328.0)	290.0 (260.0-320.0)	0.190[a]
Subfoveal, median (IQR)	262.0 (241.5-286.0)	264.0 (238.5-294.0)	0.414[a]
Choroid (μm)			
Nasal-750, mean±SD	262.2±55.1	268.5±48.0	0.439[c]
Subfoveal, median (IQR)	290.0 (253.0-338.0)	292.0 (260.5-322.0)	0.990[a]
Temporal-750, mean±SD	264.1±61.5	262.8±45.4	0.876[c]
Choroidal vascularity index, median (IQR)	0.61 (0.53-0.67)	0.63 (0.55-0.70)	0.027[d]

[a]Mann Whitney U test; [b]Chi-Square test; [c]Student t-test. IQR: Inter-quartile range; SD: Standard deviation. [d]$P<0.05$.

Table 2 Relationship between posterior segment measurements and titer in the anti-DFS70-positive group n=84

Posterior segment measurement	Anti-DFS70 titer	
	r	P^e
Macula (μm)		
Superior	-0.011	0.919
Inferior	0.076	0.492
Temporal	-0.092	0.410
Nasal	-0.055	0.619
Subfoveal	0.038	0.730
Choroid (μm)		
Nasal-750	-0.269	0.014[d]
Subfoveal	-0.263	0.016[d]
Temporal-750	-0.190	0.086
Choroidal vascularity index	-0.133	0.230

[e]Spearman correlation analysis. [d]$P<0.05$.

antibody positivity (63%) and a significant difference in mean CVI between the positive and negative groups. This seems to contrast with the significant negative correlation we observed between increasing antibody titer and decreasing subfoveal and nasal choroidal thickness (P=0.016 and P=0.014, respectively). This discrepancy requires careful interpretation and may be explained by several mutually non-exclusive hypotheses. First, the relationship might be governed by a biological threshold effect. The presence of anti-DFS70 antibodies above a certain pathogenic threshold may be sufficient to induce a stable alteration in the choroidal vascular-stromal balance. The CVI ratio effectively reflects this change. Beyond this threshold, increasing antibody titers may not provoke further proportional changes in the vascular-to-stromal ratio itself. Instead, higher antibody levels might promote a different pathological process, such as generalized tissue atrophy or ischemia, leading to the overall choroidal thinning seen in our CT data. Such threshold phenomena, where the presence of an autoantibody is more critical than its absolute concentration for initiating a specific pathological cascade, are well-recognized in antibody-mediated autoimmunity[19-20].

Second, this finding may reflect a methodological limitation of our antibody assay. Our study utilized a semi-quantitative (1+ to 3+) scoring system for antibody titers based on IIF. While standard practice, this ordinal scale offers limited granularity and may not be sensitive enough to detect a subtle, continuous dose-response relationship that might be apparent with a fully quantitative assay, such as a chemiluminescent immunoassay (CLIA) or enzyme-linked immunosorbent assay (ELISA). Future studies employing such quantitative

Table 3 Univariate and multivariate logistic regression on anti-DFS70 positivity

Parameters	Univariate			Multivariate		
	OR	95%CI	*P*	OR	95%CI	*P*
Macula (μm)						
Superior	1.00	0.99-1.00	0.441	0.98	0.96-1.00	0.021[d]
Inferior	1.01	1.00-1.02	0.120	1.04	1.02-1.07	<0.001[d]
Temporal	0.99	0.98-1.00	0.140	0.95	0.92-0.97	<0.001[d]
Nasal	1.00	1.00-1.01	0.277	1.05	1.02-1.08	<0.001[d]
Subfoveal	0.99	0.99-1.00	0.224	0.99	0.97-1.01	0.201
Choroid (μm)						
Nasal-750	1.00	0.99-1.00	0.437	0.98	0.96-1.00	0.115
Subfoveal	1.00	0.99-1.01	0.941	1.01	0.99-1.03	0.367
Temporal-750	1.00	0.99-1.01	0.875	1.01	0.99-1.02	0.410
Choroidal vascularity index	0.02	0.00-0.61	0.025	0.02	0.00-1.91	0.094

[d]$P<0.05$. OR: Odds ratio; CI: Confidence interval.

methods are necessary to clarify the true nature of the dose-response relationship between anti-DFS70 antibody burden and choroidal vascularity. In the univariate model, a reduced CVI was a statistically significant predictor of anti-DFS70 positivity (OR=0.02, *P*=0.025). However, its statistical significance was diminished (*P*=0.094) in the multivariate model that also adjusted for macular thickness parameters. In this more comprehensive model, macular thickness in the superior, inferior, temporal, and nasal quadrants emerged as strong, independent predictors of antibody status (all *P*<0.05). Statistically, this suggests that the relationship between CVI and anti-DFS70 status is confounded by, or mediated through, co-existing changes in macular thickness. However, this statistical finding has profound biological implications. It does not necessarily invalidate the importance of CVI but instead suggests a more integrated pathophysiological process. Rather than being an isolated vascular marker, the reduction in CVI may be part of a broader, subclinical chorioretinal phenotype associated with anti-DFS70 positivity. It is plausible that the presence of these antibodies, or the underlying immune dysregulation they indicate, causes concurrent changes in both the choroidal vasculature (affecting CVI) and the overlying retinal structure (affecting macular thickness). The multivariate model indicates that, within our cohort, the structural changes in the macula are a more reliable or direct statistical marker of this phenotype than the vascular changes reflected by CVI alone. These findings highlight that the ocular effects of anti-DFS70 may extend beyond a single tissue layer and emphasize the need for a multi-parameter assessment of the posterior segment. We did not report separate measurements of the total choroidal area, luminal area, and stromal area mainly because the images were not obtained *via* electronic data interchange (EDI), and the choroid-scleral border was manually identified to improve visibility. Measuring these individual areas from non-EDI images with manual segmentation could introduce variability and result in data that are not directly comparable

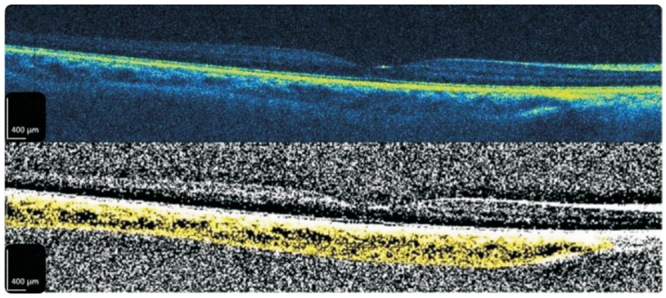

Figure 1 Choroidal vascularity index calculation *via* NiBlack thresholding method.

to studies using automated or EDI-based segmentation methods. Consequently, we opted to use CVI, which reflects the proportion of the luminal area within the total choroidal area, as it allows for a more objective comparison, along with the CT measurements taken from three points. During the study, image processing steps were implemented as a macro module, with the only user-dependent parameter being the determination of the choroidal area. As illustrated in the analysis of an anti-DFS70-positive case (Figure 1), the vascular structures appeared relatively normal, but a low index of 47% was observed during analysis with the macro module. Notably, in anti-DFS70-negative cases, subfoveal CT measurements were similar, and the CVI distribution was near normal.

Clinically, CVI is valuable non-invasive biomarker that reflects changes in choroidal vascularity in response to various inflammatory conditions. In acute phases of chorioretinal inflammation, CT increases significantly, which may also be accompanied by an increase in CVI due to heightened vascular activity[21-24]. In addition, it has been demonstrated that CT and CVI are affected in many systemic diseases with ocular manifestations, regardless of the presence of active ocular involvement[21-28]. In systemic inflammation without ocular involvement, an increase in CT without a change in CVI is a frequently observed finding[23,26]. On the contrary, chronic inflammatory diseases such as recurrent uveitis, SLE, and rheumatoid arthritis typically show a significant decrease in

CT, suggesting a potential decrease in CVI[28].

The most prominent application of anti-DFS70 antibodies in ophthalmology is autoimmune uveitis, particularly in the context of Vogt-Koyanagi-Harada (VKH) disease, which is characterized by chorioretinal inflammation[29]. The relationship between anti-DFS70 antibodies and other ocular inflammatory conditions is further evidenced by their presence in patients with idiopathic uveitis. Research has indicated that these antibodies are prevalent in sera from patients afflicted with underlying inflammatory disorders, reinforcing the idea that their detection may signify a broader dysregulation of immune responses manifesting in ocular pathology[28]. However, due to the subjective nature of HEp-2 indirect immunofluorescence assay (IFA) tests, accurate identification of the DFS pattern is crucial for its use as a biomarker in precision medicine, and misinterpretation can undermine its clinical utility. DFS70/LEDGF antibodies, which are classified as AC-2 pattern subtypes in the current classification, can often be confused with anti-dsDNA in the AC-1 pattern or anti-SSA/Ro in the AC-4 pattern[1].

A notable strength of this study is its rigorous case-control design with careful age- and sex-matching, which minimizes confounding and improves the validity of group comparisons. The relatively large sample size and high statistical power enable the detection of subtle differences in ocular parameters between anti-DFS70-positive individuals and controls. Additionally, our study uniquely addresses an important knowledge gap by focusing on a healthy population rather than patients with established autoimmune disease, providing new insights into the possible subclinical effects of anti-DFS70 antibodies. We believe that standardized imaging protocols, exclusion of participants with ocular or systemic comorbidities, and the use of objective, measurable OCT and CVI measurements further strengthened the reliability of our findings.

The study has certain technical limitations inherent to our imaging and analysis protocol. The OCT device used did not possess an EDI module, which is the current standard for better visualization of the choroid-scleral boundary and improved choroidal imaging quality. Also, our reliance on manual segmentation for defining the total choroidal area introduces a potential for increased measurement variability and decreased reproducibility compared to fully automated algorithms[30]. However, it is important to interpret this variability correctly. Our imaging and analysis protocols were standardized and applied consistently to all participants, regardless of their antibody status. Therefore, any measurement error caused by these technical factors is likely to be random, affecting both the anti-DFS70-positive and control groups similarly. In statistical epidemiology, such random error tends to bias results toward the null hypothesis and makes it harder to detect an actual difference between groups. The fact that we still found a statistically significant difference in CVI between the groups, despite these technical challenges that would typically favor a null result, suggests that the underlying biological effect is strong and might even be larger than what we observed[18]. Second, while the biometry device used provided comprehensive anterior segment measurements, it did not allow for direct lens thickness assessment, precluding evaluation of lens-specific effects previously linked to anti-DFS70 antibodies[16]. Finally, a major limitation is the cross-sectional nature of the study, which inherently restricts our ability to infer causality or understand the timeline of the observed vascular changes. Our findings provide a “snapshot in time” and cannot definitively determine whether the reduced CVI is a cause or an effect of anti-DFS70 antibody positivity. The observed association could represent several different scenarios: either the presence of anti-DFS70 antibodies directly causes structural and vascular changes in the choroid, or an unmeasured systemic factor, like a low-grade inflammatory state, independently leads to both the ocular changes and the production of anti-DFS70 antibodies. Therefore, the current data cannot be used to predict long-term clinical outcomes for these healthy individuals. Clarifying these possibilities and understanding the prognostic significance of reduced CVI in this population will require longitudinal studies that monitor both antibody status and ocular parameters over time.

In conclusion, our study identifies a novel association between anti-DFS70 antibody positivity and a subclinical chorioretinal change in otherwise healthy individuals. A significantly lower CVI marks this phenotype and changes in macular thickness. Although our cross-sectional, unilateral design and imaging limitations mean these findings are preliminary, they offer essential, hypothesis-generating evidence of potential eye involvement in people with these common autoantibodies. The complex statistical relationship seen between CVI, macular thickness, and antibody status indicates that the effects of anti-DFS70 may extend beyond the choroidal blood vessels to involve a broader response of the entire posterior segment. Future longitudinal, bilateral studies with improved-depth imaging OCT, fully quantitative antibody tests, and advanced statistical models are essential to clarify the causal pathways, assess the prognostic importance of these findings, and define the full range of the ocular manifestations of anti-DFS70-positive autoimmunity.

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Data Availability: The data of this study can be accessed upon reasonable request from the corresponding author.

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REFERENCES

1 Sanchez-Hernandez ES, Ortiz-Hernandez GL, Ochoa PT, *et al*. The nuclear dense fine speckled (DFS) immunofluorescence pattern: not all roads lead to DFS70/LEDGFp75. *Diagnostics* 2023;13(2):222.

2 Dinse GE, Zheng B, Co CA, *et al*. Anti-dense fine speckled 70 (DFS70) autoantibodies: correlates and increasing prevalence in the United States. *Front Immunol* 2023;14:1186439.

3 Santler B, Wimmer L, Schlueter B, *et al*. Anti-DFS70 antibodies are associated with atopic dermatitis and can cause misdiagnosis of connective tissue disease. *J Deutsche Derma Gesell* 2023;21(5): 464-470.

4 Tan TC, Ng C, Leong KP. Clinical utility of anti-DFS70 for identifying antinuclear antibody-positive patients without systemic autoimmune rheumatic disease. *Smedj* 2022;63(3):147-151.

5 Mahler M, Parker T, Peebles CL, *et al*. Anti-DFS70/LEDGF antibodies are more prevalent in healthy individuals compared to patients with systemic autoimmune rheumatic diseases. *J Rheumatol* 2012;39(11):2104-2110.

6 Krzemień P, Kasperczyk S, Banach M, *et al*. Relationship between anti-DFS70 autoantibodies and oxidative stress. *Biomark Insights* 2022;17.

7 Carter JB, Carter S, Saschenbrecker S, *et al*. Recognition and relevance of anti-DFS70 autoantibodies in routine antinuclear autoantibodies testing at a community hospital. *Front Med (Lausanne)* 2018;5:88.

8 Zhu HY, Chu CX, Liu ZY, *et al.* Anti-DFS70 antibodies are more prevalent in UCTD and Asian SLE patients [Preprint]. *Research Square* 2023. https://doi.org/10.21203/rs.3.rs-3374403/v1

9 Ortiz-Hernandez GL, Sanchez-Hernandez ES, Casiano CA. Twenty years of research on the DFS70/LEDGF autoantibody-autoantigen system: many lessons learned but still many questions. *Autoimmun Highlights* 2020;11(1):3.

10 Dai YX, Li EL, Chen DD, *et al*. Anti-DFS70 antibodies in systemic lupus erythematosus: prevalence in a large Chinese cohort and an unexpected association with anti-dsDNA antibodies by a long-term follow-up. *Front Immunol* 2022;13:913714.

11 Kim M, Ha MJ, Choi SY, *et al*. Choroidal vascularity index in type-2 diabetes analyzed by swept-source optical coherence tomography. *Sci Rep* 2018;8:70.

12 Iovino C, Pellegrini M, Bernabei F, *et al*. Choroidal vascularity index: an in-depth analysis of this novel optical coherence tomography parameter. *J Clin Med* 2020;9(2):595.

13 Agrawal R, Salman M, Tan KA, *et al*. Choroidal vascularity index (CVI)-a novel optical coherence tomography parameter for monitoring patients with panuveitis *PLoS One* 2016;11(1):e0146344.

14 Agrawal R, Gupta P, Tan KA, *et al*. Choroidal vascularity index as a measure of vascular status of the choroid: measurements in healthy eyes from a population-based study. *Sci Rep* 2016;6:21090.

15 Cheung CY, Ong YT, Hilal S, *et al*. Retinal ganglion cell analysis using high-definition optical coherence tomography in patients with mild cognitive impairment and Alzheimer's disease. *J Alzheimers Dis* 2015;45(1):45-56.

16 Bizzaro N, Tonutti E, Visentini D, *et al*. Antibodies to the lens and cornea in anti-DFS70-positive subjects. *Ann N Y Acad Sci* 2007;1107(1):174-183.

17 Ahuja P, Caffé AR, Holmqvist I, *et al*. Lens epithelium-derived growth factor (LEDGF) delays photoreceptor degeneration in explants of rd/rd mouse retina. *Neuroreport* 2001;12(13):2951-2955.

18 Sonoda S, Sakamoto T, Yamashita T, *et al*. Luminal and stromal areas of choroid determined by binarization method of optical coherence tomographic images. *Am J Ophthalmol* 2015;159(6):1123-1131.e1.

19 Berry CT, Frazee CS, Herman PJ, *et al*. Current advancements in cellular immunotherapy for autoimmune disease. *Semin Immunopathol* 2025;47(1):7.

20 Rosenblum MD, Remedios KA, Abbas AK. Mechanisms of human autoimmunity. *J Clin Invest* 2015;125(6):2228-2233.

21 Ong J, Zarnegar A, Corradetti G, *et al*. Advances in optical coherence tomography imaging technology and techniques for choroidal and retinal disorders. *J Clin Med* 2022;11(17):5139.

22 Betzler BK, Ding JB, Wei X, *et al*. Choroidal vascularity index: a step towards software as a medical device. *Br J Ophthalmol* 2022;106(2):149-155.

23 Motamed Shariati M, Khazaei S, Yaghoobi M. Choroidal vascularity index in health and systemic diseases: a systematic review. *Int J Retina Vitreous* 2024;10(1):87.

24 Bousquet E, Khandelwal N, Séminel M, *et al*. Choroidal structural changes in patients with birdshot chorioretinopathy. *Ocul Immunol Inflamm* 2021;29(2):346-351.

25 Evereklioglu C, Polat OA, Gulmez Sevim D, *et al*. Choroidal vascularity index and submacular choroidal thickness in patients with Behçet disease assessed with enhanced-depth OCT. *Can J Ophthalmol* 2024;59(5):e603-e611.

26 Han YE, Jo J, Kim HC, *et al*. Choroidal manifestations of non-ocular sarcoidosis: an enhanced depth imaging OCT study. *BMC Ophthalmol* 2024;24(1):199.

27 Dave TV, Jonnadula GB, Lanka P, *et al*. Choroidal vascularity index in thyroid eye disease: comparison with controls and application in diagnosing non-inflammatory active disease. *Orbit* 2022;41(1):89-96.

28 Fang A, Wang MY, Chang YC, *et al*. Investigate the change of choroidal thickness in patients with common systemic autoimmune diseases: a review. *Retina* 2025;45(10):1826-1832.

29 Yamada K, Senju S, Shinohara T, *et al*. Humoral immune response directed against LEDGF in patients with VKH. *Immunol Lett* 2001;78(3):161-168.

30 Doganay S, Doganay D, Kacmaz E. Detecting early changes in choroidal vascularity and thickness using optical coherence tomography in patients with corneal crosslinking for keratoconus. *Int J Ophthalmol* 2024;17(7):1267-1272.