Section: Ophthalmology

Original Research Article

EFFECT OF ANGIOGENESIS INHIBITOR BEVACIZUMAB /PRP ON SUBFOVEAL CHOROIDAL CHANGES AND IT'S CORRELATION TO FINAL VISUAL OUTCOMES IN DIABETIC RETINOPATHY: A PROSPECTIVE STUDY

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ABSTRACT

Background: Purpose: To evaluate changes in subfoveal choroidal thickness (SFCT) using enhanced-depth imaging optical coherence tomography (EDI-OCT) in patients with sight-threatening diabetic retinopathy (DR) before and 12 weeks after standard management, and to correlate these changes with best-corrected visual acuity (BCVA).

Materials and Methods: This prospective study enrolled 86 subjects (146 eyes) with proliferative diabetic retinopathy (PDR) or diabetic maculopathy between August 2022 and July 2023 at Government Headquarters Hospital, Cuddalore. Consecutive sampling was used. SFCT, BCVA, duration of diabetes mellitus (DM), and glycemic indices were recorded at baseline and 12-week follow-up after intravitreal anti–vascular endothelial growth factor (VEGF) therapy and/or pan-retinal photocoagulation (PRP).

Results: Mean baseline SFCT was 239 ± 41.6 µm, reducing to 202.1 ± 43.2 µm at three months ($P < 0.001$). Median logMAR BCVA improved from 0.78 (Snellen 6/36) to 0.60 (Snellen 6/24) ($P < 0.001$). SFCT positively correlated with BCVA at follow-up (rho = 0.206; P = 0.013), indicating that thicker choroid was associated with reduced vision.

Conclusion: SFCT decreases significantly after intravitreal anti-VEGF/PRP therapy and correlates with functional visual outcome. SFCT measurement by EDI-OCT can serve as a non-invasive biomarker to monitor treatment response in diabetic macular edema (DME) and proliferative DR.

Keywords: sub foveal choroidal thickness, Diabetic retinopathy, Pan- retinal Photocoagulation.

INTRODUCTION

Diabetic retinopathy (DR) remains one of the foremost causes of preventable visual impairment and blindness worldwide, with an estimated global prevalence exceeding 22% among individuals with diabetes mellitus.[1] India, which is home to over 100 million people with diabetes, is projected to witness a steep rise in DR-related visual morbidity over the next decade, underscoring the need for timely detection of early biomarkers and effective interventions. Although retinal microangiopathy has long been thought to be the defining feature of DR, new research shows that the choroid, a vital vascular layer that nourishes the outer retina, plays a critical role in the etiology and development of the condition.[2]

Vascular dropout, capillary loss, stromal oedema, and altered choroidal perfusion are among the anatomical and functional alterations in the

choroidal vasculature that are referred to as "diabetic choroidopathy".[3] The transport of oxygen and nutrients to the retinal pigment epithelium and photoreceptors may be compromised by these changes, which might exacerbate the overexpression of vascular endothelial growth factor (VEGF) brought on by ischemia leading to macular oedema or proliferative disease.[4] A non-invasive indicator of choroidal vascular health and disease activity, subfoveal choroidal thickness (SFCT) is easily measured with improved depth imaging–optical coherence tomography (EDI-OCT).[5]

Nevertheless, there is still inconsistency in the published data about the size and direction of SFCT changes in DR. Choroidal thinning has been reported in a number of cross-sectional investigations, which attribute it to autonomic dysregulation, microvascular dropout, and persistent ischemia.[6] On the other hand, some studies show choroidal thickening, which may be brought on by VEGF-mediated vascular hyperpermeability, elevated choroidal blood flow, and acute inflammatory reactions, especially when diabetic macular oedema (DME) is present.[7] Variations in research design, retinopathy stage, glycaemic management, systemic comorbidities, and ethnicity might all account for these disparities.

Intravitreal anti-VEGF injections to lessen macular oedema and panretinal photocoagulation (PRP) to reverse neovascularisation are commonly used in the treatment of sight-threatening DR. Both therapies have the capacity to alter choroidal circulation: PRP can cause localised alterations in choroidal perfusion through heat effects, while anti-VEGF medicines may decrease choroidal thickness by decreasing vascular permeability. However, there is currently no long term data assessing SFCT dynamics after these therapies, especially from Indian populations, and it is unclear how these interventions relate to visual results.[8]

The current study sought to fill these information gaps by assessing changes in subfoveal choroidal thickness over a three-month period after anti-VEGF and/or PRP therapy in eyes with diabetic retinopathy that poses a risk to vision and by establishing a correlation between SFCT changes and final best-corrected visual acuity. Comprehending these connections might aid in improving prognostic evaluation and directing customised therapy plans for individuals with advanced DR.

Objectives

Primary objective: To assess the changes in sub foveal choroidal thickness before and 12 weeks (3months) after the management with Intravitreal Bevacizumab / PRP of sight threatening diabetic retinopathy patients using optical coherence tomography(EDI-OCT).

Secondary Objective: To determine the relationship of sub foveal choroidal thickness with final visual outcome after the management of sight threatening diabetic retinopathy patients.

MATERIALS AND METHODS

Study Design and Participants

A Prospective study among the patients who presented with the features of proliferative diabetic retinopathy (PDR) and diabetic maculopathy to Department of Ophthalmology, Government Head Quarters Hospital Cuddalore, Tamilnadu.Institutional Ethical committee approval given on 1/7/22, Ref.No.12959/E4/2022

Study duration: 12 Months (August 2022 to July 2023)

Inclusion Criteria: Adults aged >18– <60 years with newly diagnosed proliferative DR (PDR) or diabetic maculopathy.

Exclusion Criteria: Prior DR treatment, vitreoretinal surgery, other retinal diseases, significant media opacities, OCT signal strength <6/10, ocular surgery within six months, high refractive error (>±6 D), systemic illnesses (hypertension, cardiac, renal), nystagmus, or congenital retinal anomalies.

Sample Size: A sample of 86 subjects needed to assess the changes in sub-foveal choroidal thickness (SFCT) using optical coherence tomography in sight threatening diabetic retinopathy patients. The expected Mean (SD) of SFCT in PDR cases was 334.59 (47.4) in reference article, 10% precision and 95% confidence interval.

Clinical Evaluation

Indirect Ophthalmoscopy, +90/+78 D lenses, intraocular pressure, anterior segment slit-lamp assessment, and BCVA LogMAR) were all part of the thorough ocular examination. The Early Treatment Diabetic Retinopathy Study (ETDRS) criteria were used to assess DR. Haemoglobin, fasting and postprandial blood sugar, HbA1c, renal parameters, and lipid profile were among the laboratory tests.

OCT Procedure

Patient is explained about the procedure and made to sit comfortably in front of the OCT with proper chin and head rest. OCT images were taken focusing on the posterior pole of retina.

The images were analysed and the sub-foveal choroidal thickness were documented.

Interventions

Eyes received treatment as clinically indicated:

- Intravitreal anti-VEGF injections (bevacizumab),
- Pan-retinal photocoagulation (PRP),
- Combination therapy.

Statistical Analysis

Data were analyzed using SPSS v28. Normality was tested with Shapiro–Wilk. Paired t-test/Wilcoxon test compared baseline and follow-up measures. Student's t-test/Mann–Whitney U assessed differences across DR severities. Correlations between SFCT and BCVA were evaluated with Spearman rank test. $P < 0.05$ was considered significant.

RESULTS

Table 1: Demographic factors of the Study Participants (n = 86)

Parameters	n (%)
Age (years)	54.3 ± 7.2
Range	40 – 75
Gender	Male: 57 (66.3)
	Female: 29 (33.7)
Laterality of DR	Unilateral: 26 (30.2)
	Bilateral: 60 (69.8)
Area of Living	Urban: 52 (60.5)
	Rural: 34 (39.5)
Occupation	Farmer: 29 (33.7)
	Business: 21 (24.4)
	Housewife: 13 (15.1)
	Teacher: 11 (12.8)
	Tailor: 6 (6.9)
	Painter: 5 (5.8)
	Carpenter: 1 (1.2)
Duration of Diabetes (years)	16.1 ± 3.9
Range	10 – 27

The study included 86 participants with a mean age of 54.3 ± 7.2 years (range 40–75). Males comprised two-thirds of the cohort (66.3%). Diabetic retinopathy was bilateral in most cases (69.8%) and unilateral in 30.2%. A majority lived in urban areas (60.5%). Farmers formed the largest occupational group (33.7%), followed by businesspersons (24.4%), housewives (15.1%), teachers (12.8%), tailors (6.9%), painters (5.8%), and one carpenter (1.2%). The mean diabetes duration was 16.1 ± 3.9 years, ranging from 10 to 27 years.

Table 2: Screening test for Diabetes mellitus

Parameters	Mean ± SD	Range
Fasting Blood Sugar (mg/dL)	143.6 ± 25.3	100 – 214
Post-prandial Blood Sugar (mg/dL)	254.8 ± 33.3	182 – 289
HbA1c (%)	9.1 ± 2.1	6 – 14.5

Screening results show poor glycemic control among participants, with mean fasting blood sugar 143.6 ± 25.3 mg/dL (range 100–214) and post-prandial glucose 254.8 ± 33.3 mg/dL (range 182–289). The mean HbA1c was 9.1 ± 2.1 %, ranging from 6 to 14.5 %, indicating chronic hyperglycemia well above recommended targets.

Table 3: Baseline Ocular Characteristics (n = 146 eyes)

Feature	n (%)
Diagnosis	
NPDR with Clinically Significant Macular Edema (CSME)	57 (39.0)
Proliferative Diabetic Retinopathy (PDR)	89 (61.0)
OCT Findings	
Diffuse Diabetic Macular Edema	68 (46.6)
Cystoid Macular Edema	35 (24.0)
Posterior Taut Hyaloid	2 (1.4)
Serous Retinal Detachment / SRF	41 (28.1)
Intervention Performed	
Anti-VEGF (Bevacizumab)	62 (42.5)
Pan-retinal Photocoagulation (PRP)	53 (36.3)
Combined Anti-VEGF + PRP	31 (21.2)

Among the 146 eyes studied, proliferative diabetic retinopathy (PDR) was more common (61.0%) than non-proliferative DR with clinically significant macular edema (39.0%). Optical coherence tomography showed diffuse diabetic macular edema in nearly half of the eyes (46.6%), followed by serous retinal detachment/sub-retinal fluid (28.1%), cystoid macular edema (24.0%), and posterior taut hyaloid (1.4%). Treatment included intravitreal anti-VEGF injections in 42.5% of eyes, pan-retinal photocoagulation in 36.3%, and combined therapy in 21.2%, reflecting the advanced disease stage in many patients.

Table 4: Visual acuity at baseline and follow up: 3-Month Follow-up

BCVA	Baseline	3monthsfollow-up	*P*-value*
LogMAR Median (Snellen's VA)	0.78 (6/36)	0.60 (6/24)	
IQR	0.48 – 1	0.48 – 0.78	**<0.001**

*-Paired Samplet - test/Wilcox on Sign Rank test; Bold face indicates statistical significance

Table.4 shows that, the visual acuity was converted into log MAR values and the log MAR visual acuity was compared between Baseline and 3 months follow-up.

- The median logMAR BCVA was 0.78 and the respective Snellen's VA was 6/36 in the Baseline.
- The median logMAR BCVA was 0.60 and the respective Snellen's VA was 6/24 in the 3 months follow-up.
- There was an improvement found between two visits and the difference was statistically significant (*P*-value <0.001

Table 5: SFCT at baseline and follow up:

SFCT	Baseline(□m)	3 months follow-up(□m)	P-value*
Mean±SD	239 ± 41.6	202.1 ± 43.2	**<0.001**
Range	153 – 341	25 – 325	

*-Paired Samplet-test / Wilcoxon Sign Rank test; Bold face indicates statistical significance

Table.5 shows that, the SFCT was compared between Baseline and 3 months follow- up. The Mean ± SD of SFCT was 239±41.6□m and 202.1±43.2□m in the Baseline and3 months follow-up. The SFCT was significantly reduced over the time period and that was statistically significant (*P*-value <0.001).

Table 6: Visual outcome after treatment / 3 months follow-up

Outcome	(n=146), n (%)
No difference	67 (45.9)
Worsened	24 (16.4)
Improved	55 (37.7)

Table.6 shows that, only 16.4% of the study participants have worsened visual outcome in the 3 months follow-up. 45.9% of them having same visual acuity in both Baseline and 3 months follow-up. 37.7% of them were having improvement.

Table 7: Correlation of SFCT and Final Visual Outcome

Correlation	n (%) or Value
Correlation Between SFCT and logMAR BCVA	Spearman rho = **0.206**; P = **0.013**

Scatter plot shows, there was positive relationship between SFCT and Visual acuity at 3 months follow-up. That indicates the SFCT was increasing the visual acuity get worsening. The relationship was statistically significant (rho0.206;P-value 0.013).

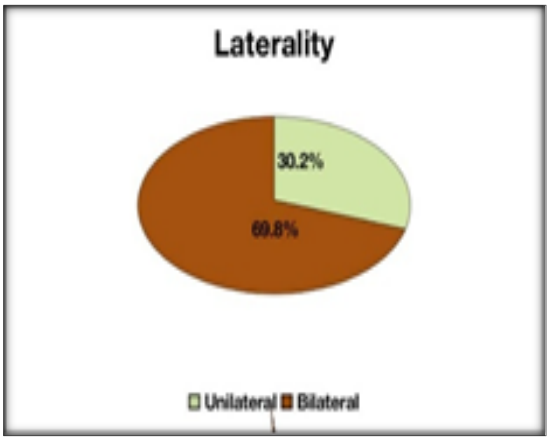

Figure 1A: Pie chart for gender distribution

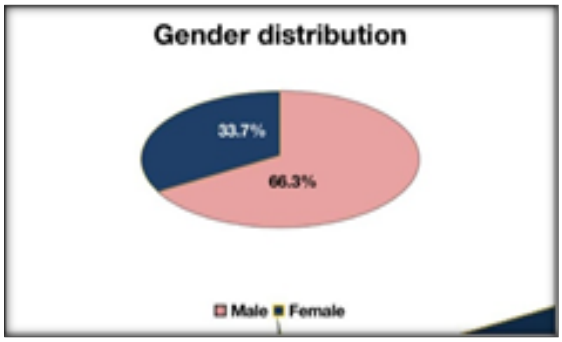

Figure 1B: Pie chart for laterality

Figure 1C: Occupation distribution

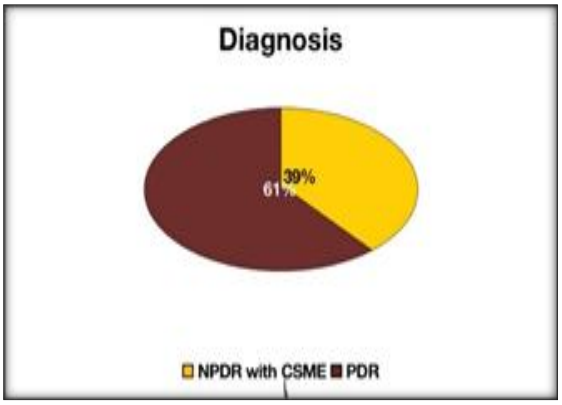

Figure 2A: Pie chart for diagnosis

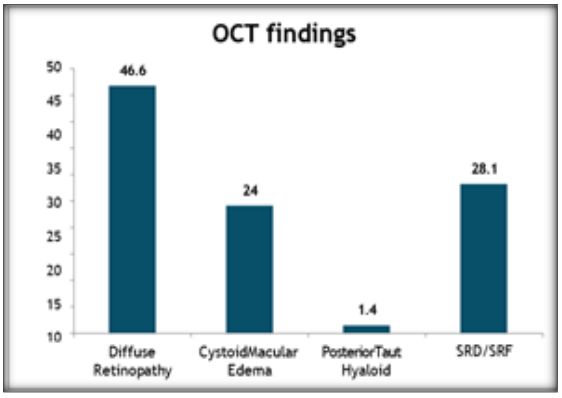

Figure 2B: Bar graph for OCT findings

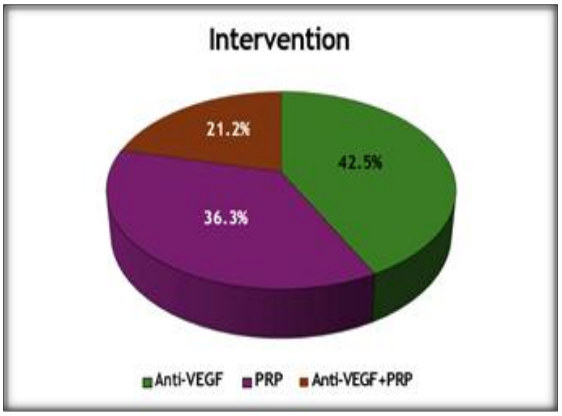

Figure 2C: Pie chart for intervention

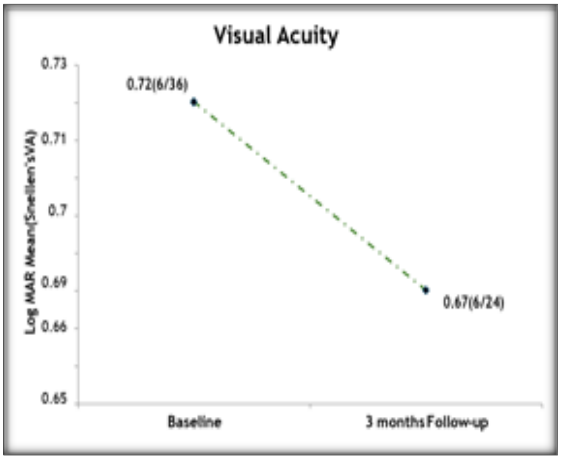

Figure 3. Line chart for visual acuity

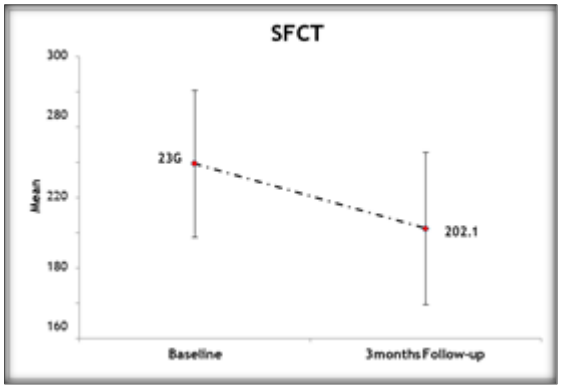

Figure 4: Line chart for SFCT

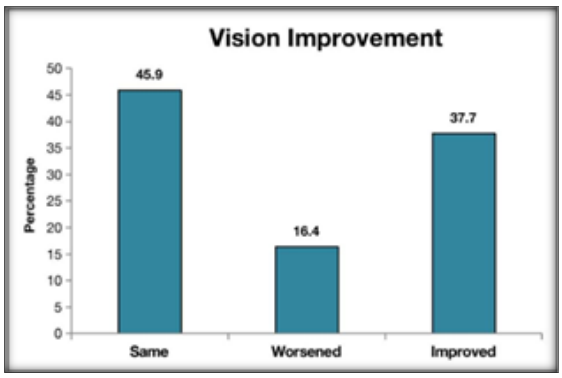

Figure 5: vision improvement at followup

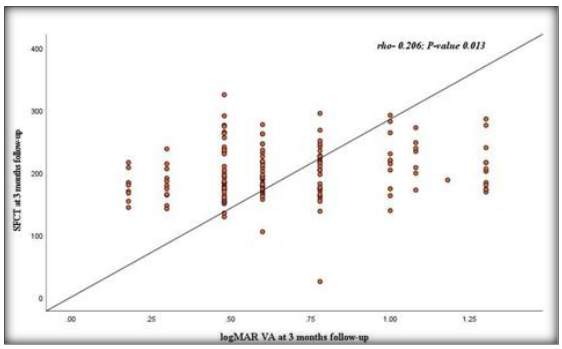

Figure 7: Scatter plot showing the relationship between SFCT and VA at follow-up

DISCUSSION

In patients with diabetic retinopathy (DR), the current study offers a comprehensive assessment of baseline ocular features, therapy treatments, systemic metabolic management, demographic variables, and short-term results. The results emphasize how structural retinal alterations, chronic diabetes, and inadequate glycemic management interact to influence visual prognosis.

Demographic and systemic profile

In line with the average beginning of sight-threatening DR documented in Indian and international research, where the majority of afflicted persons are in their fifth or sixth decade of life, our cohort's mean age was 54.3 7.2 years (range 40–75). Lee et al. (2015).[9] The male preponderance (66.3%) is consistent with previous population-based data that indicated a greater frequency of DR

in males, which may be due to variations in health-seeking behavior, hormonal impacts, and risk factors associated with lifestyle. Rani et al., (2021).[10] The systemic character of diabetic microangiopathy and the necessity of binocular screening were highlighted by the almost 70% of subjects who had bilateral illness.

The majority (60.5%) lived in urban areas, which is indicative of the increased prevalence of diabetes in urban India due to sedentary lifestyles and eating habits. The fact that a sizable percentage of people (33.7%) are farmers raises the possibility of occupational hurdles to treatment adherence and routine follow-up in semi-urban or peri-urban areas. The substantial correlation between the advancement of DR and the chronicity of the illness is further supported by the mean duration of diabetes, which is 16.1 ± 3.9 years. Anjana RM et al. (2019).[11]

The following biochemical values support inadequate systemic control: HbA1c of 9.1 ± 2.1%, postprandial level of 254.8 mg/dL, and mean fasting blood sugar of 143.6 mg/dL. These numbers above the American Diabetes Association's recommended threshold of less than 7% HbA1c, corroborating the idea that inadequate glycaemic management hastens the incidence and severity of retinopathy. DCCT Research Group, 2016.[12]

Ocular characteristics and interventions

Proliferative diabetic retinopathy (PDR) was present in 61% of the eyes at baseline, whereas non-proliferative DR with clinically significant macular oedema (CSME) was present in 39% of the eyes. This high percentage of advanced illness is consistent with findings from Southeast Asian and Indian tertiary-care populations, where late presentation is typical.[10] Diffuse diabetic macular oedema (46.6%) and serous retinal detachment/sub-retinal fluid (28.1%) were the most common morphologies seen by optical coherence tomography (OCT), and both conditions are known to be associated with poor initial vision. Mitchell et al., (2018).[13]

The severity of the illness was mirrored in the treatment patterns: 32.3% underwent pan-retinal photocoagulation (PRP), 21.2% received combination therapy, and 42.5% received intravitreal anti-VEGF (bevacizumab). These ratios align with current standard-of-care guidelines that suggest PRP for PDR and anti-VEGF for center-involving macular oedema. Flaxel et al., (2020).[14] The combined approach has been shown to enhance regression of neovascularization while reducing injection burden.

Visual and structural outcomes

The median logMAR visual acuity at three months showed a considerable functional improvement, rising from 0.78 (≈6/36 Snellen) to 0.60 (≈6/24) ($p < 0.001$). These advantages align with PRP and anti-VEGF randomised trials in similar populations. Gadkari SS et al.(2016).[2]

The subfoveal choroidal thickness (SFCT) decreased significantly from 239 ± 41.6 µm to 202.1 ± 43.2 µm ($p < 0.001$) according to spectral-domain OCT. Following therapy, a decrease in SFCT has been regarded as a proxy for better choroidal perfusion and less inflammatory drive. Gupta C et al., (2018).[5]

Significantly, SFCT and final log MAR visual acuity were found to be positively correlated (Spearman rho = 0.206; $p = 0.013$), indicating that thicker baseline SFCT indicated worse eyesight at follow-up. This finding is consistent with publications that relate disease activity and leakage to choroidal thickening. Regatieri et al., (2012; Tan et al., (2018).[7,15] While the correlation coefficient is modest, it reinforces the potential of SFCT as a non-invasive biomarker for prognosis.

Clinical implications and limitations

In order to stop the development of PDR and vision-threatening macular edema, the study emphasizes the critical necessity for early identification and stricter metabolic management. Including OCT-based choroidal measures in regular evaluation might assist identify eyes that are more likely to have negative results. Among the limitations include the single-center design, which may restrict generality, the comparatively brief three-month follow-up, and the absence of stratification by systemic comorbidities such dyslipidaemia or hypertension.

CONCLUSION

The reliable, non-invasive imaging of the choroid offered by enhanced-depth and swept-source OCT allows for the measurement of the subfoveal choroidal thickness (SFCT). In this study, there was a substantial correlation between SFCT and the severity of diabetic retinopathy (DR) and the presence of diabetic macular oedema (DME). Progressive choroidal thickness with rising DR or DME is indicative of underlying diabetic choroidopathy. Since the choroid feeds the outer retina, its study offers crucial information for early detection and following the development of the illness.

The differences across studies are likely due to systemic and ocular factors as age, blood pressure, axial length, refractive error, diurnal fluctuation, and prior intravitreal anti-VEGF therapy and /or panretinal photocoagulation (PRP). The choroidal vascularity index (CVI), which is a dependable measure that drastically decreases with degradation, is the ratio of luminal to total choroidal area. Our findings validate the use of SFCT as a biomarker for assessing therapeutic response and predicting visual outcomes in diabetic eye disease by showing that it sharply declines after anti-VEGF or PRP treatment.

Limitation

This study is subject to several limitations. First, if those with a naturally thin choroid at baseline do not

exhibit further discernable thinning throughout follow-up, there could be a floor effect. Second, choroidal thickness is known to vary during the day, even with efforts to employ consistent scheduling. Readings may be impacted by this physiological variation. Inconsistent follow-up visits and individuals' varying glycemic control further introduce bias and might jeopardise the reliability of longitudinal comparisons. In addition, several ocular and systemic factors, such as age, length of diabetes, axial length, refractive status, and elevated HbA1c levels, might alter choroidal thickness on their own and act as confounders.

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