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급성 중심성 장액맥락망막병증에서 은행잎 추출물의 효과: 다기관 후향적 연구

Effect of Ginkgo biloba Extract on Anti-vascular Endothelial Growth Factor Treatment Requirement and Chronicity in Acute Central Serous Chorioretinopathy: A Multicenter Retrospective Study

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Purpose: To evaluate whether oral Ginkgo biloba extract (GBE) is associated with reduced anti-vascular endothelial growth factor (anti-VEGF) treatment requirement and chronicity in patients with acute central serous chorioretinopathy (CSC).

Methods: This multicenter retrospective cohort study included treatment-naïve patients with acute CSC from two academic hospitals between January 2022 and December 2024. Patients were classified into a GBE group (Ginexin® 80 mg twice daily, 28 eyes) and a non-GBE group (31 eyes). Best-corrected visual acuity (BCVA), central macular thickness (CMT), subfoveal choroidal thickness (SFCT), and subretinal fluid (SRF) were evaluated at baseline, 6 months, and 12 months. Multivariable logistic regression analysis was performed, adjusting for age, sex, baseline BCVA, and baseline CMT.

Results: A total of 59 patients (59 eyes) were included. The GBE group showed a significantly lower rate of anti-VEGF treatment compared to the non-GBE group (35.7% vs. 83.9%, $p < 0.001$) and fewer injections (3.20 ± 1.87 vs. 5.08 ± 3.07, $p = 0.035$). GBE use was independently associated with reduced anti-VEGF requirement (adjusted odds ratio [aOR] 0.15, 95% confidence interval [CI] 0.04–0.60; $p = 0.008$). Chronicity was lower in the GBE group (39.3% vs. 74.2%, $p = 0.014$), though not significant after adjustment (aOR 0.41, 95% CI 0.12–1.46; $p = 0.170$). Residual SRF was significantly lower in the GBE group at 6 and 12 months. SFCT reduction from baseline to 12 months was significantly greater in the GBE group (-49.2 ± 23.4 vs. -24.9 ± 48.4 μm, $p = 0.016$), remaining significant after adjusting for baseline SFCT ($p = 0.019$).

Conclusions: GBE use was associated with a reduced need for anti-VEGF treatment and greater SFCT reduction in patients with acute CSC, suggesting a possible role in modulating choroidal congestion. Further prospective studies are warranted to confirm these findings.

Keywords: Central serous chorioretinopathy; Choroid; Ginkgo extract; Subretinal fluid; Vascular endothelial growth factor

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Introduction

Central serous chorioretinopathy (CSC) is a retinal disorder characterized by serous detachment of the neurosensory retina, primarily associated with choroidal vascular hyperpermeability and dysfunction of the retinal pigment epithelium (RPE) barrier. It typically affects middle-aged individuals and presents with decreased visual acuity, metamorphopsia, and impaired contrast sensitivity. Although acute CSC is generally considered a self-limiting condition with spontaneous resolution of subretinal fluid (SRF) within 3–4 months in many cases, its clinical course is variable [1-5].

Importantly, a substantial proportion of patients develop persistent or recurrent SRF, leading to chronic CSC, which is associated with photoreceptor damage, RPE alterations, and long-term visual impairment. Furthermore, macular neovascularization (MNV) may arise in a subset of cases, particularly in chronic or atypical presentations, necessitating treatment with anti-vascular endothelial growth factor (anti-VEGF) agents [6-8]. These disease courses contribute to increased treatment burden and variability in visual prognosis, highlighting the need for strategies that can modulate disease activity in the early stage.

Ginkgo biloba extract (GBE) is a standardized herbal preparation containing flavonoids and terpenoids, which exhibit antioxidant, anti-inflammatory, and vasoregulatory properties. Experimental and clinical studies have demonstrated that GBE can improve microvascular circulation, enhance retinal and choroidal blood flow, and reduce oxidative stress–related cellular damage [9-12]. These mechanisms are of particular relevance to CSC, in which choroidal vascular dysregulation and oxidative stress are considered key contributors to disease pathophysiology.

Based on these observations, GBE may have a potential role in modulating disease activity and reducing the need for invasive treatments in CSC. However, clinical evidence regarding its impact on treatment requirement and disease course in acute CSC remains limited. Therefore, the purpose of this study was to evaluate whether oral GBE is associated with reduced anti-VEGF treatment requirement and chronicity in patients with acute CSC.

Materials and Methods

Study design and patients

This multicenter retrospective cohort study was conducted at two university hospitals (Uijeongbu St. Mary's Hospital and Chung-Ang University Gwangmyeong Hospital) in Republic of Korea. Medical records of patients diagnosed with acute CSC between January 2022 and December 2024 were reviewed. All clinical data were collected up to December 31, 2025, and only patients with a minimum follow-up duration of 12 months from the time of diagnosis were included in the analysis. The study was approved by the Institutional Review Boards of the Uijeongbu St. Mary's Hospital and Chung-Ang University Gwangmyeong Hospital (UC25RIDI0100 and 2601-297-002). The requirement for informed consent was waived due to the retrospective nature of the study.

Inclusion and exclusion criteria

Patients were included if they were newly diagnosed with acute CSC and had at least 1 year of follow-up. Acute CSC was defined as the presence of SRF involving the macula with symptom duration less than 6 months. At baseline, all patients underwent optical coherence tomography (OCT) and optical coherence tomography angiography (OCT-A); fluorescein angiography (FA) and/or indocyanine green angiography were additionally performed when clinically indicated to exclude neovascular age-related macular degeneration (AMD), polypoidal choroidal vasculopathy, or other chorioretinal disorders. Eyes with evidence of MNV, neovascular AMD, polypoidal choroidal vasculopathy, or other chorioretinal disorders were excluded. Exclusion criteria included: (1) prior treatment for CSC (including photodynamic therapy or anti-VEGF injection), (2) presence of other macular diseases (e.g., AMD, diabetic macular edema), (3) evidence of chronic CSC at baseline, and (4) insufficient clinical data.

Treatment groups

Patients were divided into two groups according to the use of GBE. The GBE group received oral GBE, while the non-GBE group did not receive GBE. The GBE group received oral GBE (Ginexin®; SK Chemicals; 80 mg twice daily) for at least 6 months, and treatment duration was extended at the discretion of the treating physician based on clinical response. Treatment decisions, including GBE administration, were made at the discretion of the treating physician.

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Clinical evaluation

Baseline demographic and clinical data, including age, sex, best-corrected visual acuity (BCVA), and central macular thickness (CMT), were collected. BCVA was converted to logarithm of the minimum angle of resolution (logMAR) for analysis. OCT was used to evaluate the presence of SRF and measure CMT. Subfoveal choroidal thickness (SFCT) was measured manually using the caliper function of the OCT device at the point of maximum choroidal thickness beneath the foveal center on enhanced depth imaging-OCT. Clinical outcomes were assessed at baseline, 6 months, and 12 months. In addition, baseline corticosteroid exposure (systemic, inhaled, intranasal, or topical use within the preceding 6 months), hypertension, diabetes mellitus, hyperlipidemia, fellow eye involvement, and symptom duration prior to presentation were recorded from medical records.

Outcome measures

The primary outcome was the requirement for anti-VEGF treatment during the follow-up period. Anti-VEGF treatment was administered only when MNV was identified using multimodal imaging, including FA and OCT-A. MNV was defined as the presence of a flow signal corresponding to a neovascular network on OCT-A, with or without leakage on FA, consistent with type 1 MNV beneath the RPE. Standardized imaging protocols were applied at both participating centers.

Secondary outcomes included: (1) number of anti-VEGF injections, (2) presence of SRF at each follow-up visit, (3) overall clinical improvement or worsening, and (4) chronicity.

Overall clinical improvement and worsening were assessed at the final follow-up visit (12 months after diagnosis). Overall clinical improvement was defined as complete resolution of SRF with stable or improved BCVA, whereas clinical worsening was defined as persistence or increase of SRF and/or deterioration in BCVA at the final follow-up visit.

Anti-VEGF treatment protocol

The anti-VEGF agent used was bevacizumab (1.25 mg/0.05 mL), administered promptly after confirmation of MNV. After the initial injection, patients were followed using OCT and clinical examination. Additional injections were administered on a pro re nata basis when persistent or recurrent SRF, increased retinal thickness, new hemorrhage, or evidence of active MNV was observed.

Statistical analysis

Continuous variables are presented as mean ± standard deviation, and categorical variables as number (percentage). Intergroup comparisons were performed using the independent t-test for continuous variables and the chi-square test for categorical variables. Paired t-test was used for within-group comparisons over time. When the expected cell count was less than 5, Fisher's exact test was used instead of the chi-square test. For the comparison of SFCT change at 12 months, analysis of covariance (ANCOVA) was additionally performed with baseline SFCT as a covariate.

To evaluate the association between GBE use and clinical outcomes, multivariable logistic regression analysis was performed. Variables with clinical relevance or a p-value < 0.1 in univariate analysis were included in the multivariable model to adjust for potential confounding factors. In particular, age, sex, baseline BCVA, and baseline CMT were included as covariates in the multivariable model. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were calculated. Given the retrospective nature of this study, no formal sample size calculation was performed. Therefore, the findings should be interpreted as exploratory and hypothesis-generating.

A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences software 25.0 (IBM Corp.).

Results

Baseline characteristics

A total of 59 eyes from 59 patients were included, with 28 eyes in the GBE group and 31 eyes in the non-GBE group. The mean age was significantly lower in the GBE group than in the non-GBE group (44.21 ± 9.40 vs. 49.97 ± 10.55 years, $p = 0.031$). Baseline BCVA was also better in the GBE group (0.12 ± 0.16 vs. 0.24 ± 0.24 logMAR, $p = 0.024$). There were no significant differences in sex distribution or baseline CMT between the groups. No significant differences were observed between the two groups in the prevalence of systemic comorbidities, including corticosteroid use, hypertension, diabetes mellitus, and hyperlipidemia (all $p > 0.05$), although hyperlipidemia showed a borderline difference (7.1% vs. 25.8%, $p = 0.084$). Baseline SFCT did not differ significantly between groups (397.54 ± 85.11 vs. 388.03 ±

103.87 μm, $p = 0.701$). Fellow eye involvement was observed only in the non-GBE group (16.1% vs. 0%, $p = 0.054$), and symptom duration prior to presentation was comparable between groups (3.39 ± 2.90 vs. 4.10 ± 3.32 weeks, $p = 0.388$) (Table 1).

Changes in BCVA, CMT and SRF resolution

At baseline, BCVA was significantly better in the GBE group compared to the non-GBE group (0.12 ± 0.16 vs. 0.24 ± 0.24 logMAR, $p = 0.024$). This difference persisted throughout the follow-up period, with the GBE group maintaining better BCVA at both 6 months (0.11 ± 0.15 vs. 0.23 ± 0.26, $p = 0.035$) and 12 months (0.11 ± 0.17 vs. 0.23 ± 0.27, $p = 0.045$).

Table 1. Baseline characteristics of patients with acute central serous chorioretinopathy

Variable	GBE (n = 28)	Non-GBE (n = 31)	*p*-value
Age (years)	44.21 ± 9.40	49.97 ± 10.55	0.031*
Sex, male:female	23:5	24:7	0.900†
Baseline BCVA (logMAR)	0.12 ± 0.16	0.24 ± 0.24	0.024*
Baseline CMT (μm)	391.11 ± 114.64	416.48 ± 151.65	0.469*
Steroid use	0 (0)	2 (6.5)	0.493‡
Hypertension	7 (25.0)	10 (32.3)	0.578‡
Diabetes	3 (10.7)	5 (16.1)	0.709‡
Hyperlipidemia	2 (7.1)	8 (25.8)	0.084‡
Subfoveal choroidal thickness (μm)	397.54 ± 85.11	388.03 ± 103.87	0.701*
Fellow eye involvement	0 (0)	5 (16.1)	0.054‡
Symptom duration (weeks)	3.39 ± 2.90	4.10 ± 3.32	0.388*

Values are presented as mean ± standard deviation, number only, or number (%).
GBE = Ginkgo biloba extract; BCVA = best-corrected visual acuity; CMT = central macular thickness.
*Independent t-test; †Chi-square test; ‡Fisher's exact test.

Table 2. Changes in BCVA, CMT, and SRF over time

Variable		GBE (n=28)	Non-GBE (n=31)	*p*-value
BCVA (logMAR)	Baseline	0.12 ± 0.16	0.24 ± 0.24	0.024*
	6 months	0.11 ± 0.15	0.23 ± 0.26	0.035*
	Δ (baseline→6 months)	-0.004 ± 0.097	-0.009 ± 0.172	0.892†
	1 year	0.11 ± 0.17	0.23 ± 0.27	0.045*
	Δ (baseline→1 year)	-0.006 ± 0.099	-0.008 ± 0.240	0.964†
CMT (μm)	Baseline	391.11 ± 114.64	416.48 ± 151.65	0.469*
	6 months	286.1 ± 98.7	295.5 ± 136.6	0.766*
	Δ (baseline→6 months)	-105.0 ± 114.0	-121.0 ± 157.1	0.659†
	1 year	284.3 ± 83.2	292.5 ± 95.1	0.724*
	Δ (baseline→1 year)	-106.9 ± 97.3	-123.9 ± 178.2	0.655†
SFCT (μm)	Baseline	397.54 ± 85.11	388.03 ± 103.87	0.701*
	6 months	367.6 ± 82.9	371.8 ± 97.7	0.858*
	Δ (baseline→6 months)	-30.0 ± 21.7	-16.2 ± 34.5	0.070†
	1 year	348.3 ± 78.5	363.1 ± 98.1	0.523*
	Δ (baseline→1 year)	-49.2 ± 23.4	-24.9 ± 48.4	0.016†
Presence of SRF (%)	Baseline	100	100	
	6 months	32.1	67.7	0.014‡
	1 year	17.9	51.6	0.015‡

Values are presented as mean ± standard deviation.
BCVA = best-corrected visual acuity; CMT = central macular thickness; SRF = subretinal fluid; GBE = Ginkgo biloba extract.
*Independent t-test (absolute values at each timepoint); †Independent t-test (between-group comparison of change from baseline, Δ); ‡Chi-square test.

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However, the magnitude of BCVA change from baseline did not differ significantly between the two groups at either 6 months (-0.004 ± 0.011 vs. -0.009 ± 0.226, p = 0.892) or 12 months (-0.006 ± 0.099 vs. -0.008 ± 0.240, p = 0.964), indicating comparable functional improvement over time (Table 2, Fig 1A).

CMT decreased in both groups during follow-up. In the GBE group, mean CMT decreased from 391.11 ± 114.64 μm at baseline to 286.1 ± 98.7 μm at 6 months and 284.3 ± 83.2 μm at 12 months. Similarly, in the non-GBE group, CMT decreased from 416.48 ± 151.65 μm to 295.5 ± 136.6 μm and 292.5 ± 95.1 μm at 6 months and 12 months, respectively. The degree of CMT reduction was not significantly different between the groups at either time point (p = 0.659 at 6 months and p = 0.655 at 12 months), suggesting that anatomical improvement in retinal thickness occurred similarly in both groups (Table 2, Fig 1B).

All eyes presented with SRF at baseline. During follow-up, the proportion of eyes with residual SRF decreased in both groups; however, resolution occurred more rapidly and to a greater extent in the GBE group. At 6 months, residual SRF was observed in 32.1% of eyes in the GBE group compared to 67.7% in the non-GBE group (p = 0.014). This difference remained significant at 12 months, with residual SRF in 17.9% of the GBE group versus 51.6% of the non-GBE group (p = 0.015). A significantly lower proportion of

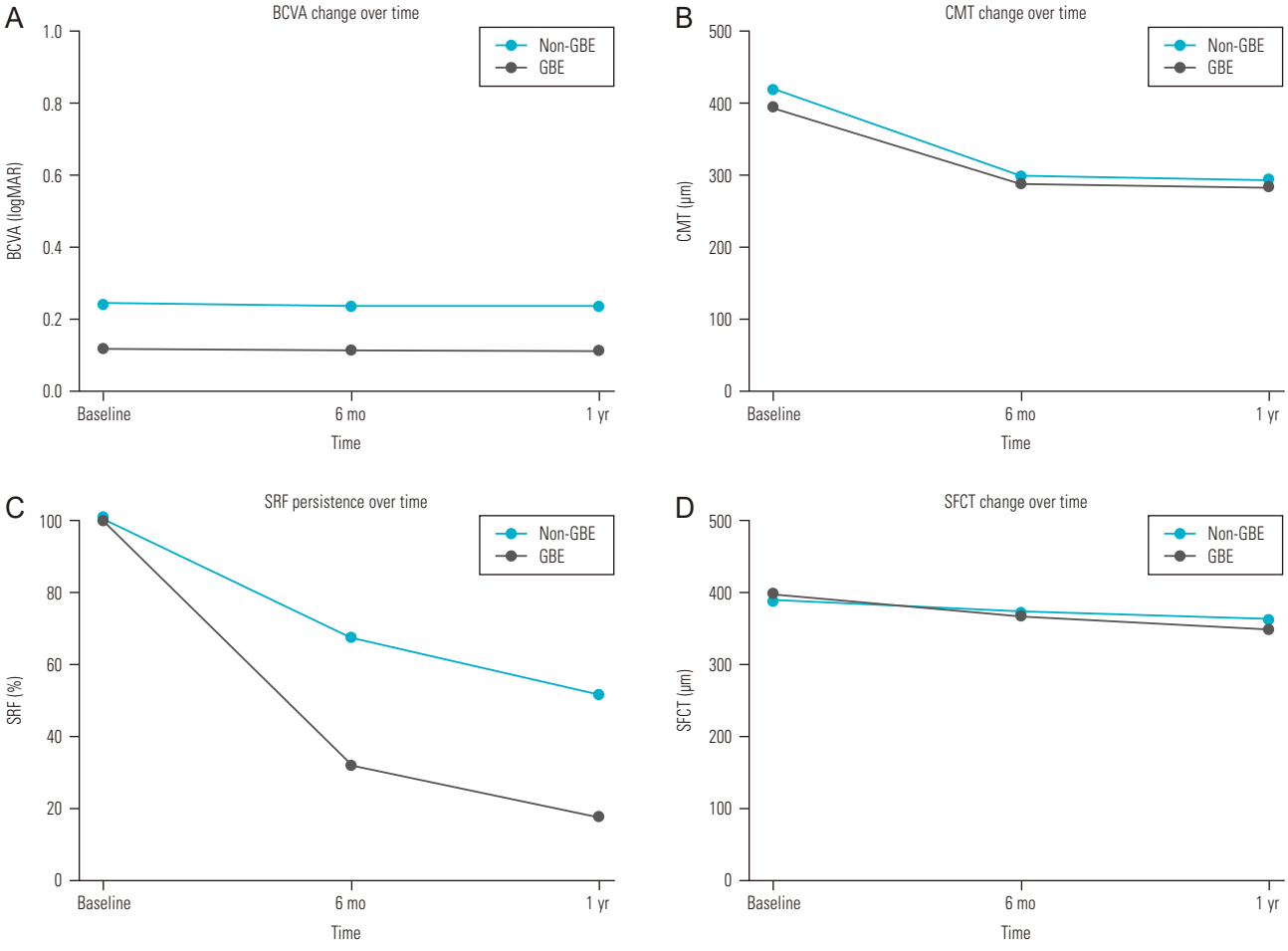


Figure 1. Changes in BCVA, CMT, and SRF over time. (A) Changes in BCVA over time. BCVA remained relatively stable in both groups, with consistently better values in the GBE group. (B) Changes in CMT over time. CMT decreased in both groups during follow-up without significant intergroup differences. (C) Changes in the proportion of eyes with SRF over time. The proportion of eyes with residual SRF was lower in the GBE group at both 6 and 12 months. (D) Changes in SFCT over time. SFCT decreased progressively in both groups, with a significantly greater reduction in the GBE group at 12 months. BCVA = best-corrected visual acuity; CMT = central macular thickness; SRF = subretinal fluid; GBE = Ginkgo biloba extract; SFCT = subfoveal choroidal thickness.

residual SRF was observed in the GBE group at both 6 and 12 months (Table 2, Fig 1C).

Changes in SFCTs

SFCT decreased progressively in both groups during follow-up. SFCT was 397.5 ± 85.1 μm at baseline, 367.6 ± 82.9 μm at 6 months, and 348.3 ± 78.5 μm at 12 months in the GBE group, compared with 388.0 ± 103.9 μm, 371.8 ± 97.7 μm, and 363.1 ± 98.1 μm, respectively, in the non-GBE group. No significant between-group difference was observed in absolute SFCT at any timepoint (p = 0.701, 0.858, and 0.523 at baseline, 6 months, and 12 months, respectively). However, the magnitude of SFCT reduction from baseline was significantly greater in the GBE group at 12 months (-49.2 ± 23.4 vs. -24.9 ± 48.4 μm, p = 0.016), while the difference at 6 months did not reach statistical significance (-30.0 ± 21.7 vs. -16.2 ± 34.5 μm, p = 0.070). This between-group difference at 12 months remained significant after adjusting for baseline SFCT using ANCOVA (adjusted difference, -22.95 μm; 95% CI, -41.99 to -3.91; p = 0.019) (Fig 1D).

Clinical outcomes and multivariable analysis

At the 12-month follow-up visit, the GBE group demonstrated a significantly higher rate of overall clinical improvement compared to the non-GBE group (85.7% vs. 45.2%, p = 0.003), whereas the rate of clinical worsening was lower in the GBE group. The proportion of eyes requiring anti-VEGF treatment during the follow-up period was significantly lower in the GBE group than in the non-GBE group (35.7% vs. 83.9%, p < 0.001). In addition, among eyes that received anti-VEGF treatment, the mean number of injections was significantly lower in the GBE group (3.20 ± 1.79 vs. 5.08 ± 3.07, p = 0.035) (Table 3).

The proportion of eyes classified as chronic CSC was lower in the GBE group compared to the non-GBE group (39.3% vs. 74.2%, p = 0.014) (Table 3). In multivariable logistic regression analysis adjusting for potential confounding variables, GBE use was associated with a lower likelihood of requiring anti-VEGF treatment (aOR 0.15, 95% CI 0.04–0.60; p = 0.008). In contrast, although the point estimate for chronicity was lower in the GBE group, the association did not reach statistical significance after adjustment (aOR 0.41, 95% CI 0.12–1.46; p = 0.170). The aORs and corresponding CIs for anti-VEGF requirement and chronicity are presented in Fig. 2. Full results of the multivariable models, including aORs for all covariates, are presented in Supplementary Table 1.

Discussion

In this multicenter retrospective study, the main findings can be summarized as follows. First, the use of GBE was associated with a significantly lower requirement for anti-VEGF treatment in patients with acute CSC, and this association remained significant after adjustment for potential confounding variables. Second, the proportion of eyes with residual SRF during follow-up was lower in the GBE group, particularly at 6 and 12 months. Third, although the rate of chronicity was lower in the GBE group in unadjusted analysis, this association did not remain statistically significant after multivariable adjustment. Finally, functional and anatomical outcomes, including BCVA and CMT, were comparable between the two groups.

Among these findings, the most clinically relevant observation was the reduced requirement for anti-VEGF treatment in the GBE group. In the context of CSC, anti-VEGF therapy is typically reserved for cases complicated by MNV, which is associated with a more severe or prolonged disease course [3,8,13]. Therefore, a lower need for anti-VEGF treatment may reflect reduced disease activity or a lower likelihood of progression to MNV-related complications.

CSC is generally considered a self-limiting disease; however, a subset of patients experiences persistent or recurrent SRF, leading to chronic CSC and potential visual impairment [2]. In this regard, early modulation of disease activ-

Table 3. Clinical outcomes, including anti-VEGF treatment and chronicity, in the GBE and non-GBE groups

Clinical outcome at 12 months	GBE (n = 28)	Non-GBE (n = 31)	p-value
Overall improvement	24 (85.7)	14 (45.2)	0.003*
Overall worsening	4 (14.3)	17 (54.8)	
Anti-VEGF use	10 (35.7)	26 (83.9)	<0.001*
Injection number	3.20 ± 1.87	5.08 ± 3.07	0.035†
Chronicity	11 (39.3)	23 (74.2)	0.014*

Values are presented as number (%) or mean ± standard deviation.
anti-VEGF = anti-vascular endothelial growth factor; GBE = Ginkgo biloba extract.
*Chi-square test; †Independent-t test.

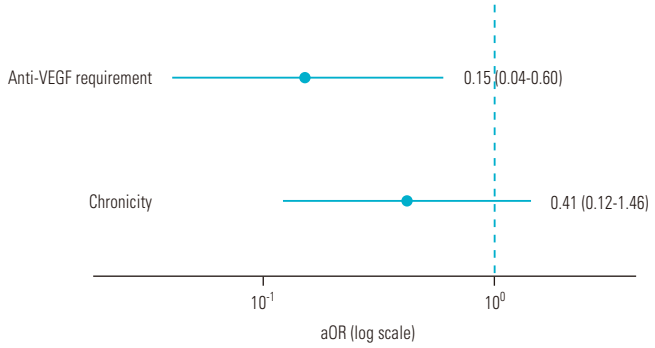
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ity may be clinically meaningful. The lower proportion of residual SRF observed in the GBE group during follow-up suggests that GBE may be associated with a more favorable anatomical course, although causality cannot be established in this retrospective analysis.

The biological plausibility of these findings may be supported by the known pharmacologic properties of GBE. GBE has been reported to exert antioxidant and anti-inflammatory effects, as well as to improve microvascular circulation and choroidal blood flow [9,11]. Given that CSC is closely associated with choroidal vascular dysfunction and oxidative stress, these mechanisms may contribute to stabilization of the RPE and reduction of fluid leakage [5]. Although the exact mechanisms underlying the observed associations remain to be elucidated, these effects provide a potential explanation for the clinical findings.

One hypothesis regarding the pathophysiology of CSC suggests that choroidal hyperpermeability and congestion lead to choroidal dysfunction [1,14,15]. This dysfunction subsequently induces RPE abnormalities and breakdown, resulting in fluid leakage beneath the neurosensory retina [2,15]. Recently, studies have proposed that increased scleral thickness or rigidity triggers this choroidal congestion. Specifically, a thickened or rigid sclera elongates the intrascleral path of the vortex veins and increases resistance to choroidal venous outflow. This elevation in resistance exerts back pressure on Haller's layer, leading to its dilation [2,14,15]. Previous studies have demonstrated that GBE improves peripheral blood circulation and enhances blood flow in the ophthalmic artery; furthermore, it has been reported to improve choroidal circulation in murine models [9,11,12]. Rather than simply augmenting arterial inflow, the vasoactive and rheologic effects of GBE—including improved microcirculatory perfusion and reduced blood viscosity—may facilitate venous outflow and alleviate the elevated choroidal venous resistance proposed in the venous overload choroidopathy model, thereby reducing Haller's layer congestion rather than exacerbating it. In addition to its potential hemodynamic effects on venous outflow, GBE may exert a complementary vasoprotective action at the cellular level. Furthermore, an in vitro study using human vascular endothelial cells revealed that GBE protects against ischemic injury induced by hypoxia and angiotensin-II hypersecretion. In that study, GBE exhibited vasoprotective effects by suppressing endothelin secretion, attenuating the reduction of mitochondrial membrane potential, and mitigating the influx of calcium ions Ca^{2+} [16]. Notably, in the present cohort, the GBE group demonstrated a significantly greater reduction in SFCT at 12 months compared with the non-GBE group ($p = 0.016$ by independent t-test; $p = 0.019$ after adjusting for baseline SFCT) which is consistent with attenuation of choroidal congestion rather than its aggravation, and lends empirical support to this mechanistic hypothesis.

A notable finding in the present study is the relatively high rate of anti-VEGF treatment and the lower rate of spontaneous improvement observed in the non-GBE group



Clinical outcome	aOR (GBE)	95% CI	*p*-value*
Anti-VEGF requirement	0.15	0.04-0.60	0.008
Chronicity	0.41	0.12-1.46	0.170

Figure 2. Adjusted associations between GBE use and clinical outcomes. Forest plot showing aORs and 95% CIs for anti-VEGF requirement and chronicity according to GBE use. GBE = Ginkgo biloba extract; anti-VEGF = anti-vascular endothelial growth factor; aOR = adjusted odds ratio; CI = confidence interval.

compared to what has been reported in previous studies of acute CSC. This discrepancy may be explained by the characteristics of the study population. First, this study reflects a real-world clinical setting at academic hospitals, where patients with more persistent or symptomatic disease are more likely to be followed longitudinally. Patients with mild disease who experience early spontaneous resolution may be underrepresented, particularly given the inclusion of patients with at least 1 year of follow-up. Second, anti-VEGF treatment in this study was administered only when MNV was identified using multimodal imaging. Therefore, the relatively high rate of anti-VEGF treatment likely reflects the inclusion of patients with more complicated or progressive disease rather than overtreatment. This interpretation is further supported by the relatively low rate of spontaneous resolution observed in the non-GBE group, suggesting that the study cohort represents a higher-risk subset of acute CSC rather than the general population. Taken together, these factors suggest that the study population may represent a subset of acute CSC with a higher risk of persistence or progression, which should be considered when interpreting the results. In this context, the observed reduction in anti-VEGF treatment requirement in the GBE group is noteworthy, although it should be interpreted with caution. The potential influence of underlying disease severity on treatment outcomes cannot be fully excluded, and further prospective studies are needed to clarify the role of GBE in different clinical settings.

In contrast, although the rate of chronicity was lower in the GBE group in the unadjusted analysis, this association was not statistically significant after multivariable adjustment. This discrepancy may be explained by limited statistical power due to the relatively small sample size, as well as the multifactorial nature of CSC chronicity. Factors such as disease duration, recurrence patterns, and individual susceptibility may influence long-term outcomes and were not fully accounted for in the present study.

Several limitations of this study should be acknowledged. First, the retrospective design introduces the possibility of selection bias, as treatment decisions, including GBE administration, were made at the discretion of the treating physician. Importantly, baseline differences between the groups, particularly younger age and better baseline BCVA in the GBE group, may have influenced the observed outcomes. These differences raise the possibility that patients with a more favorable natural disease course were more likely to receive GBE. Although these variables were adjusted for in the multivariable analysis, residual confounding cannot be completely excluded and should be considered when interpreting the results. Second, the sample size was relatively small, which may limit the generalizability of the findings and the statistical power for certain outcomes, particularly chronicity. Finally, unmeasured confounding factors, such as psychosocial stress or sleep quality, could not be fully controlled.

In conclusion, GBE use was associated with a reduced need for anti-VEGF treatment in patients with acute CSC and showed a tendency toward reduced chronicity. These findings suggest that GBE may serve as a potential adjunctive therapeutic option in the early management of CSC. Future prospective randomized controlled trials are warranted to determine the optimal treatment duration, patient selection criteria, and long-term efficacy of GBE in this population.

Conflicts of Interest

The authors declare no conflicts of interest relevant to this article.

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Author Contribution

Conception (J.H.J); Design (S.H.L., J.H.J); Data acquisition (All authors); Analysis (S.H.L); Interpretation (J.H.J); Writing (S.H.L); Review (J.H.J); Final approval of the article (All authors)

Availability of Data and Material

The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Supplementary Table 1. Multivariable logistic regression analysis for anti-VEGF treatment requirement and chronicity

Variable	Anti-VEGF treatment aOR (95% CI)	*p*-value	Chronicity aOR (95% CI)	*p*-value
GBE use (vs. non-GBE)	0.15 (0.04–0.60)	0.008	0.41 (0.12–1.46)	0.170
Age (per year)	1.04 (0.95–1.12)	0.408	1.08 (1.00–1.17)	0.058
Sex (male vs. female)	0.92 (0.17–5.11)	0.925	0.72 (0.15–3.49)	0.682
Baseline BCVA (per 0.1 logMAR)	1.98 (1.14–3.44)	0.015	1.69 (1.04–2.73)	0.033
Baseline CMT (per 10 μm)	1.05 (0.98–1.13)	0.134	1.02 (0.96–1.09)	0.468

anti-VEGF = anti-vascular endothelial growth factor; aOR = adjusted odds ratio; CI = confidence interval; GBE = Ginkgo biloba extract; BCVA = best-corrected visual acuity; CMT = central macular thickness.
Both models were adjusted for GBE use, age, sex, baseline BCVA, and baseline CMT.

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