

Treatment Trends of Diabetic Macular Edema in Korea (TRACK) Study: A Prospective Multicenter Study

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Purpose: To evaluate real-world functional and anatomical outcomes, treatment patterns, and ocular examination trends in diabetic macular edema (DME) in Korea.

Methods: A prospective, multicenter, observational study was conducted at 17 hospitals (2017–2022) involving adults with DME. Patients were categorized into center-involving DME (CI-DME) and non-CI-DME groups based on optical coherence tomography findings. Serial changes in best-corrected visual acuity (BCVA), central subfoveal thickness (CST), and treatment and examination patterns were recorded at baseline and follow-up visits (6, 12, 18, and 24 months), and analyzed using linear mixed models and paired t-tests.

Results: A total of 209 participants (81 female patients, 38.8%; mean age, 60.2 ± 10.8 years) were enrolled. Over 24 months, 10 of 68 non-CI-DME patients (14.7%) developed CI-DME. CST significantly decreased in the CI-DME group (from 419 µm at

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baseline to 343 μm , $p = 0.001$), whereas BCVA remained unchanged in both groups. Throughout the 2-year period, the average number of anti-vascular endothelial growth factor (anti-VEGF) injections was 3.1 ± 3.6 , while steroid injections averaged 0.7 ± 1.5 . The CI-DME group received significantly more anti-VEGF injections compared to the non-CI-DME group (3.8 ± 3.9 vs. 2.0 ± 2.8 , $p = 0.004$). Additionally, the CI-DME group had more frequent visits (15.8 vs. 11.3, $p = 0.017$) and optical coherence tomography examinations (9.7 vs. 7.4, $p = 0.023$). The number of anti-VEGF injections decreased in the CI-DME group over time, while the number of visits decreased in both groups.

Conclusions: In real-world clinical practice in Korea, the treatment and monitoring frequency for DME was lower than in major clinical trials, potentially contributing to suboptimal visual outcomes.

Key Words: Diabetic macular edema, Korea, Therapeutics

Diabetic macular edema (DME) is a leading cause of vision impairment in patients with diabetic retinopathy and a significant global healthcare burden [1,2]. The increasing prevalence of diabetes worldwide has contributed to a rising incidence of DME, necessitating effective treatment strategies to prevent visual deterioration and maintain quality of life [3]. Current treatment options for DME primarily include intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections, corticosteroids, and laser photocoagulation, each with distinct efficacy and safety profiles [4–7].

While randomized controlled trials have demonstrated the effectiveness of anti-VEGF agents in improving visual and anatomical outcomes, real-world evidence suggests that treatment patterns and patient adherence often differ from clinical trial settings [8,9]. Variability in treatment regimens, injection frequency, and patient response in real-world practice may impact long-term outcomes [10]. Additionally, the economic burden of DME management, including treatment costs, clinic visits, and patient adherence, highlights the importance of understanding healthcare resource utilization [11].

This study aims to evaluate real-world treatment patterns for DME, assess functional and anatomical outcomes, and analyze healthcare resource utilization trends in South Korea. By providing insights into real-world clinical practice, this research seeks to bridge the gap between clinical trial data and real-world data, ultimately guiding more effective and sustainable management strategies for DME.

Materials and Methods

Ethics statement

This prospective cohort study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (No. B-1601-330-307). All participants provided written informed consent. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Study design and setting

This prospective, observational study was conducted at 17 hospitals in South Korea from January 2017 to June 2022. The key inclusion criteria required participants to be aged 20 years or older with a diagnosis of type 1 or type 2 diabetes and evidence of DME confirmed by spectral-domain optical coherence tomography (OCT) and fluorescein angiography. Patients were categorized into center-involving DME (CI-DME) and non-center-involving DME (non-CI-DME) groups based on OCT findings. The CI-DME group included eyes with retinal thickening or hard exudates within 500 μm of the foveal center and a central subfield thickness (CST) ≥ 300 μm within the 1-mm central subfield on OCT. The non-CI-DME group included eyes with retinal thickening of at least one disc diameter located ≥ 500 μm from the foveal center, CST ≤ 300 μm within 1-mm central subfield on OCT, and retinal thickening of ≥ 400 μm located ≥ 500 μm from the foveal center. The Spectralis OCT (Heidelberg Engineering) was used for 110 patients, 80 with the DRI Triton OCT (Topcon), and 19

with the Cirrus OCT system (Carl Zeiss Meditec). Segmentation errors on OCT were reviewed and manually corrected when present to ensure accurate assessment of DME status and retinal thickness measurements. Key exclusion criteria included prior intraocular surgery, and other ocular or systemic conditions that could interfere with study outcomes. A full list of inclusion and exclusion criteria, along with the criteria for group classification, is provided in the Supplementary Fig. 1.

Ocular examinations, visits, and treatments were conducted at the discretion of retinal specialists at each insti-

tution. Data were recorded at baseline screening (visit 1) and at 6 months (visit 2), 12 months (visit 3), 18 months (visit 4), and 24 months (visit 5). At visit 1, demographic data, history of ocular treatments, best-corrected visual acuity (BCVA) in letters, and OCT findings including CST, were collected. Demographic data were collected, including age, sex, smoking, and comorbidities. During follow-up visits, the number of visits, treatment history including anti-VEGF, steroid, focal laser, and panretinal photocoagulation, and findings of ophthalmic examinations, including BCVA, and CST were documented.

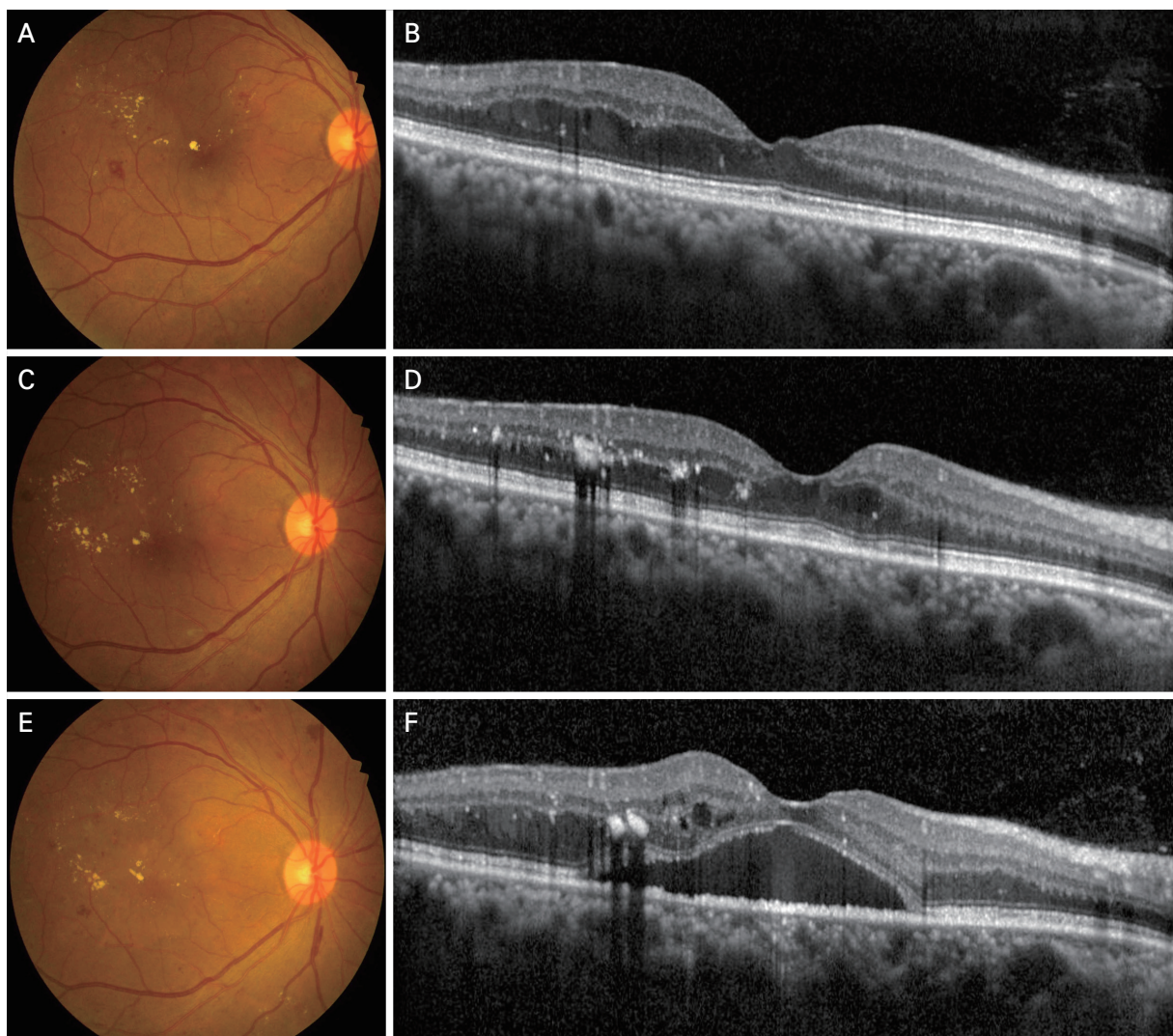


Fig. 1. A representative case of non-center-involving diabetic macular edema (non-CI-DME) during the 2-year follow-up in a 55-year-old patient. (A, B) At presentation, hard exudates and retinal hemorrhages were observed, with non-CI-DME and a best-corrected visual acuity (BCVA) of 86 letters and central subfoveal thickness (CST) of 294 μm in the right eye. (C, D) One year later, intraretinal fluid and multiple hyperreflective foci appeared, with a BCVA decrease to 71 letters and CST of 304 μm . (E, F) Two years later, severe subretinal fluid accumulation was noted, with a CST of 468 μm and a BCVA of 73 letters. During the 2-year period, the patient received two aflibercept injections, four bevacizumab injections, and one focal laser treatment.

Statistical analysis

Serial changes in variables were compared between the two groups using linear mixed models. The group and visit were included as fixed effects, with patient-specific random intercepts and an autoregressive correlation structure of order 1. Paired *t*-tests were used for comparisons between visits within each group. Bonferroni correction was applied for multiple comparisons of the values. All statistical analyses were performed using R ver. 4.4.2 (R Foundation for Statistical Computing). We considered $p < 0.05$ as statistically significant throughout our analysis.

Results

A total of 209 participants were enrolled (81 women [38.8%] and 128 men [61.2%]), with a mean age of 60.2 ± 10.8 years. CST was higher in the CI-DME group than in the non-CI-DME group ($419.0 \pm 115.9 \mu\text{m}$ vs. $279.4 \pm 45.1 \mu\text{m}$, $p < 0.001$) (Table 1). Of the 209 participants at visit 1, 165 remained for visit 2, 149 for visit 3, 124 for visit 4, and 124 for visit 5, and data on these patients were included in the analysis (Table 2). Among the 68 participants with non-CI-DME at baseline, 10 (14.7%) developed CI-DME during the follow-up (Fig. 1A–1F).

A linear mixed model analysis showed no significant interaction between visit and group for BCVA ($p = 0.085$), while significant interaction for CST ($p < 0.001$), indicating different longitudinal trends between the two groups (Table 3).

Table 1. Baseline characteristics

Characteristic	Total (n = 209)	CI-DME group (n = 141)	Non-CI-DME group (n = 68)	<i>p</i> -value*
Sex				0.063
Female	81 (38.8)	48 (34.0)	33 (48.5)	
Male	128 (61.2)	93 (66.0)	35 (51.5)	
Age (yr)	60.2 ± 10.8	60.0 ± 10.4	60.5 ± 11.7	0.786
Smoking	90 (43.1)	62 (44.0)	28 (41.2)	0.816
HbA1c (%)	7.8 ± 1.6	7.8 ± 1.6	8.0 ± 1.6	0.338
Laterality (right eye)	120 (57.4)	81 (57.4)	39 (57.4)	>0.999
Refraction (D)	-0.5 ± 2.2	-0.6 ± 2.1	-0.5 ± 2.3	0.790
BCVA (letter)	63.0 ± 19.1	61.1 ± 19.3	66.7 ± 18.2	0.055
Central subfoveal thickness (μm)	371.3 ± 118.0	419.0 ± 115.9	279.4 ± 45.1	<0.001
Intraocular pressure (mmHg)	15.7 ± 8.4	16.1 ± 9.9	14.9 ± 4.0	0.210
Comorbidity				
Hypertension	83 (39.7)	55 (39)	28 (41.2)	0.881
Hyperlipidemia	68 (32.5)	38 (27)	30 (44.1)	0.020
Stroke	11 (5.3)	7 (5.0)	4 (5.9)	>0.999
Angina	9 (4.3)	4 (2.8)	5 (7.4)	0.253
Previous treatment				-
Anti-VEGF	64 (30.6)	47 (33.3)	17 (25.0)	
Steroid injection	6 (2.9)	4 (2.8)	2 (2.9)	
Focal laser	1 (0.5)	1 (0.7)	0 (0)	
Panretinal photocoagulation	65 (31.1)	37 (26.2)	28 (41.2)	

Values are presented as number (%) or mean $\pm$ standard deviation.

CI-DME = center-involving diabetic macular edema; HbA1c = glycated hemoglobin; D = diopters; BCVA = best-corrected visual acuity; VEGF = vascular endothelial growth factor.

*Student *t*-test and chi-square test used for continuous and categorical variables, respectively.

Table 2. Number of follow-up patients per visit

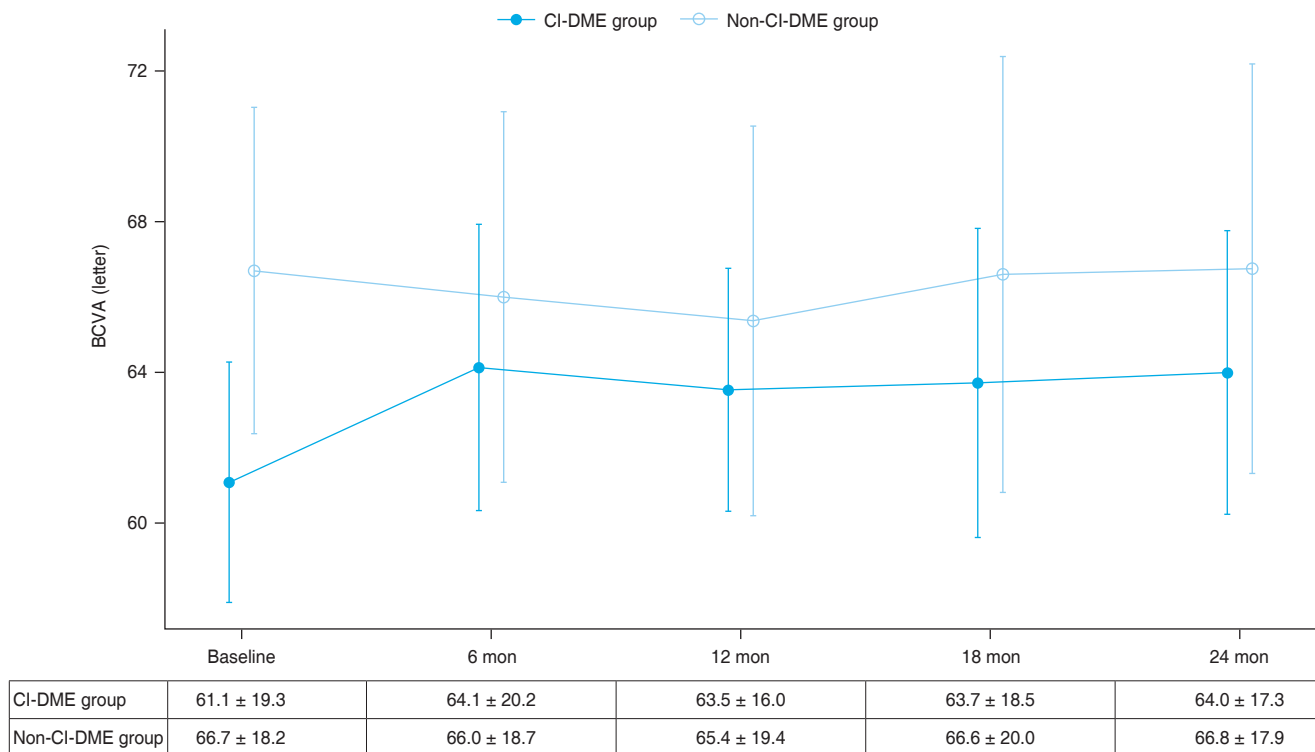
Group	Visit 1 (baseline)	Visit 2 (at 6 mon)	Visit 3 (at 12 mon)	Visit 4 (at 18 mon)	Visit 5 (at 24 mon)
CI-DME	141	109	95	78	82
Non-CI-DME	68	56	54	46	42
Total	209	165	149	124	124

CI-DME = center-involving diabetic macular edema.

Table 3. Results of linear mixed modeling

Variable	β Coefficient	Standard error	<i>p</i> -value
BCVA (letter)			
Group	-5.84	3.16	0.066
Visit	-0.98	0.58	0.091
Group $\times$ visit	1.25	0.72	0.085
Central subfoveal thickness (μ m)			
Group	144.35	18.90	<0.001
Visit	6.93	4.52	0.126
Group $\times$ visit	-27.24	5.67	<0.001

A significant group and visit interaction (group $\times$ visit) indicates differing rates of change in CI-DME compared to non-CI-DME. BCVA = best-corrected visual acuity; CI-DME = center-involving diabetic macular edema.

**Fig. 2.** Change of best-corrected visual acuity (BCVA). CI-DME = center-involving diabetic macular edema.

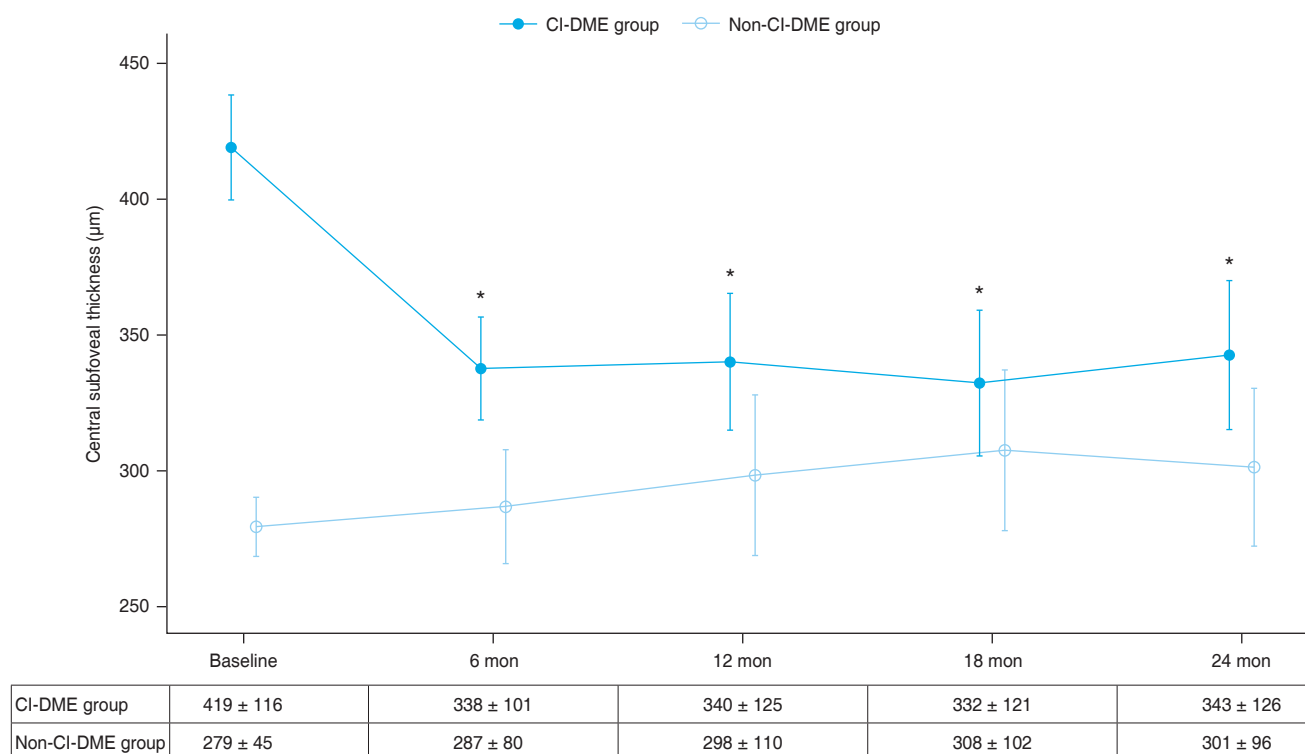


Fig. 3. Change of central subfoveal thickness. CI-DME = center-involving diabetic macular edema. * $p < 0.05$.

In the CI-DME group, the mean BCVA changed from 61.1 ± 19.3 letters at baseline to 64.0 ± 17.3 letters at visit 5 ($p > 0.999$). In the non-CI-DME group, the mean BCVA changed from 66.7 ± 18.2 letters at baseline to 66.8 ± 17.9 letters at visit 5 ($p = 0.661$) (Fig. 2). In the CI-DME group, 89 patients were treatment-naïve and 52 were previously treated group. The mean BCVA did not significantly change in either subgroup (treatment-naïve: 59.2 ± 20.9 at visit 1 vs. 63.6 ± 17.7 letters at visit 5, $p > 0.999$; previously treated: 64.7 ± 15.5 vs. 64.5 ± 17.1 letters, $p > 0.999$). A similar pattern was observed in the non-CI-DME group (treatment-naïve [$n = 45$]: 65.3 ± 20.1 vs. 66.7 ± 19.5 letters, $p = 0.703$; previously treated [$n = 23$]: 69.5 ± 13.5 vs. 66.9 ± 15.9 letters, $p > 0.999$). In the CI-DME group, the mean CST significantly decreased from 419 ± 116 μm at baseline to 338 ± 101 μm at visit 2 ($p < 0.001$), 340 ± 125 μm at visit 3 ($p < 0.001$), 332 ± 121 μm at visit 4 ($p < 0.001$), and 343 ± 126 μm at visit 5 ($p = 0.001$) (Figs. 3, 4A–4F).

Over the 2-year period, the total number of anti-VEGF injections was 3.1 ± 3.6 , while steroid injections were 0.7 ± 1.5 (Table 4). The CI-DME group received significantly more anti-VEGF injections than the non-CI-DME group (3.8 ± 3.9 vs. 2.0 ± 2.8 , $p = 0.004$). Among patients with CI-

DME, 10 of 141 (7.1%) received three to five anti-VEGF loading injections, while in the non-CI-DME group, 2 of 68 (2.9%) received the same treatment. Focal laser treatment was performed more frequently in the non-CI-DME group (14 [20.6%] vs. 5 [3.5%], $p < 0.001$). The CI-DME group had more frequent visits (15.8 ± 7.3 vs. 11.3 ± 8.1 , $p = 0.017$) and underwent OCT imaging (9.7 ± 4.2 vs. 7.4 ± 3.9 , $p = 0.023$) more often over the 2-year period.

The number of anti-VEGF injections decreased over the follow-up period only in the CI-DME group, while steroid injections showed no change in either group (Fig. 5A, 5B, and Supplementary Table 1). The number of visits significantly decreased over the follow-up period in both groups, while the number of OCT examinations decreased only in the non-CI-DME group (Fig. 6A–6C and Supplementary Table 2).

Discussion

In this study, we reported the functional and anatomical outcomes of DME patients in multiple institutions in Korea, as well as their treatment and examination patterns.

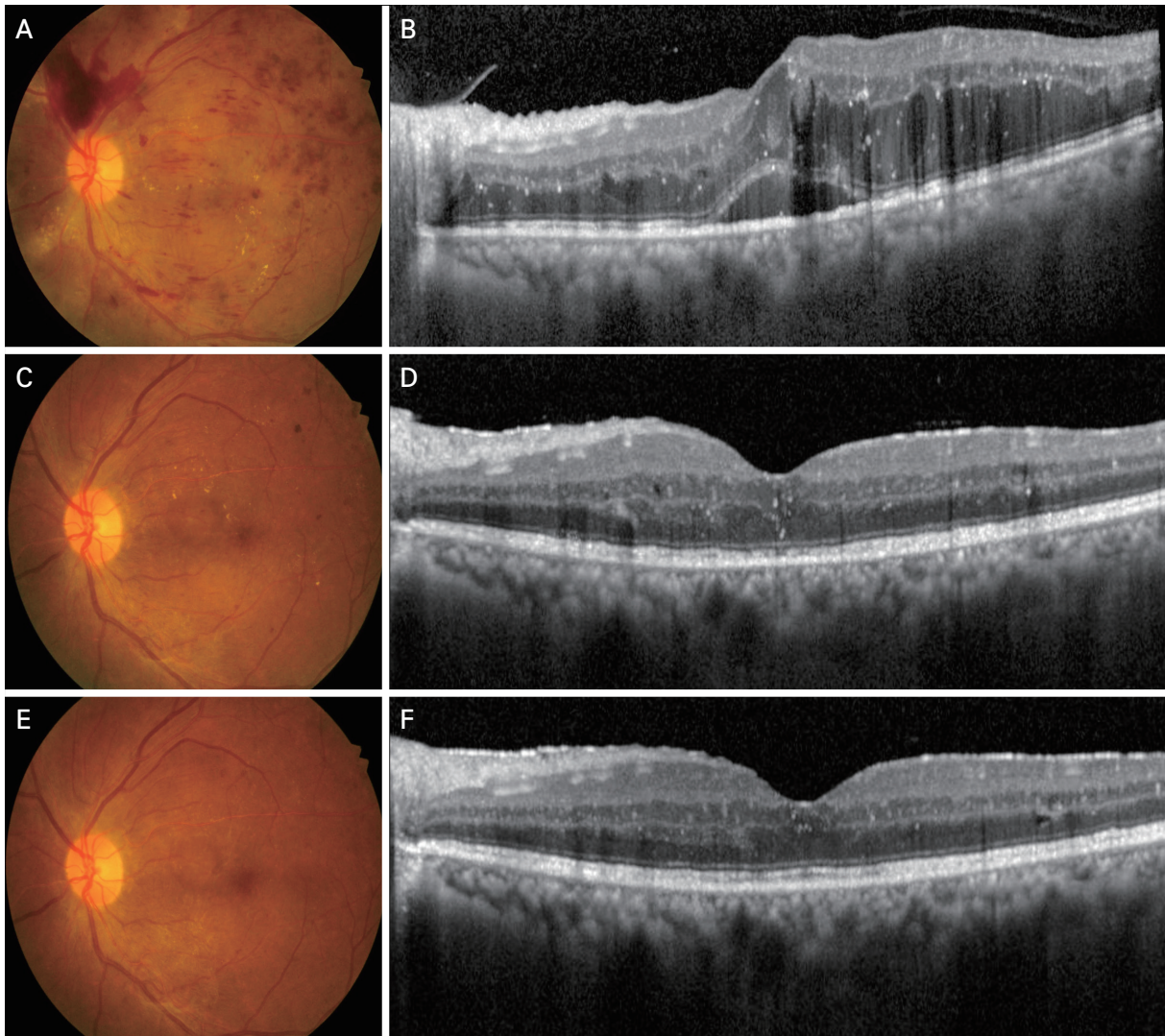


Fig. 4. A representative case of center-involving diabetic macular edema (CI-DME) during the 2-year follow-up in a 57-year-old patient. (A, B) At presentation, multiple retinal hemorrhages and large center-involving DME were observed in her left eye, with a best-corrected visual acuity (BCVA) of 72 letters and a central subfoveal thickness (CST) of 595 μm . (C, D) One year later, the retinal hemorrhages resolved, and the DME improved, with a BCVA of 69 letters and a CST of 365 μm . (E, F) Two years later, the fovea was nearly flat, with a CST of 342 μm and a BCVA of 70 letters. During the 2-year period, the patient received panretinal photocoagulation, 3 aflibercept injections, and 11 bevacizumab injections.

The CI-DME group showed a significant reduction in CST compared to baseline, which was well maintained over the 2-year period. The BCVA slightly improved in the CI-DME group, although the change did not reach statistical significance. This functional outcome is somewhat disappointing, as it is poorer than not only the results from clinical trials but also those from other real-world studies. The DRCR.net Protocol T trial showed gains of +12.8, +12.3, and +10.0 letters at 2 years for eyes treated with aflibercept, ranibizumab, and bevacizumab, respectively [12]. Similarly, the VISTA/VIVID trial reported gains of +10.3

to +11.7 letters at 3 years for eyes treated with aflibercept [13]. Recent real-world studies on DME treatment have reported visual gains of approximately 3.2 to 8.2 letters at 1 year [10,14–16]. The primary reason for this difference is that the number of injections in our cohort was significantly lower compared to other studies. In clinical trials, anti-VEGF injections were typically administered on an every 4- or 8-week schedule, resulting in a significantly higher number of injections compared to real-world studies [13,17,18]. Real-world injection numbers tend to be lower than clinical trials, often 3.9 to 7.9 injections in year 1, then

Table 4. The cumulative treatment and examination frequency until year 1 and year 2

Variable	Total (n = 209)	CI-DME group (n = 141)	Non-CI-DME group (n = 68)	p-value
Anti-VEGF injection				
At 1 yr	1.8 ± 2.2	2.2 ± 2.3	1.1 ± 1.7	0.001
At 2 yr	3.1 ± 3.6	3.8 ± 3.9	2.0 ± 2.8	0.004
Steroid injection				
At 1 yr	0.4 ± 0.9	0.5 ± 1.0	0.2 ± 0.7	0.036
At 2 yr	0.7 ± 1.5	0.9 ± 1.8	0.4 ± 1.0	0.056
Focal laser treatment				
At 1 yr	13 (6.2)	1 (0.7)	12 (17.6)	<0.001
At 2 yr	19 (9.1)	5 (3.5)	14 (20.6)	<0.001
Panretinal photocoagulation				
At 1 yr	36 (17.2)	26 (18.4)	10 (14.7)	0.635
At 2 yr	41 (19.6)	27 (19.1)	14 (20.6)	0.952
No. of visits				
At 1 yr	7.8 ± 4.3	8.5 ± 4.1	6.7 ± 4.5	0.028
At 2 yr	14.2 ± 7.9	15.8 ± 7.3	11.3 ± 8.1	0.017
Fundus photography				
At 1 yr	4.1 ± 2.8	4.3 ± 2.7	3.6 ± 3.0	0.198
At 2 yr	7.1 ± 5.4	7.9 ± 5.4	5.7 ± 5.1	0.096
OCT imaging				
At 1 yr	4.9 ± 2.3	5.2 ± 2.3	4.2 ± 2.2	0.025
At 2 yr	8.9 ± 4.2	9.7 ± 4.2	7.4 ± 3.9	0.023
Fluorescein angiography				
At 1 yr	27 (12.9)	24 (17.0)	3 (4.4)	0.020
At 2 yr	37 (17.7)	27 (19.1)	10 (14.7)	0.552

Values are presented as mean ± standard deviation or number (%).

CI-DME = center-involving diabetic macular edema; VEGF = vascular endothelial growth factor; OCT = optical coherence tomography.

declining in subsequent years [10,14–16,19]. In our cohort, the number of anti-VEGF injections was 1.8 in the first year and 3.1 over 2 years. Specifically, in the CI-DME group, the injection frequency was 2.2 in the first year and 3.8 over 2 years. This number is lower than the injection frequency reported in other studies, indicating the possibility that patients in our cohort were undertreated. Similar to our result, a real-world data from Japan showed that a group receiving anti-VEGF therapy for DME had a mean of 3.8 anti-VEGF injections over 2 years, with CST improvement but no significant visual acuity gain [20]. One of the reasons for the lower injection frequency in real-world data may be the time and financial burden on patients [21]. Additionally, in South Korea, insurance criteria

for DME treatment (a limit of 14 injections per patient and a CST ≥300 μm) may encourage physicians to prefer a as-needed regimen. Future studies incorporating socioeconomic data and healthcare system are warranted to better understand the factors underlying low treatment and monitoring frequencies.

Secondly, our study included a more heterogeneous patient population than clinical trials or other real-world studies, which may have contributed to the poorer visual outcomes. Since one-third of patients are known to have an incomplete response to anti-VEGF therapy, the 75 of 209 patients (36%) in our cohort with a history of previous treatment likely influenced the poor outcomes [22]. Subgroup analysis within the treatment-naïve patient group

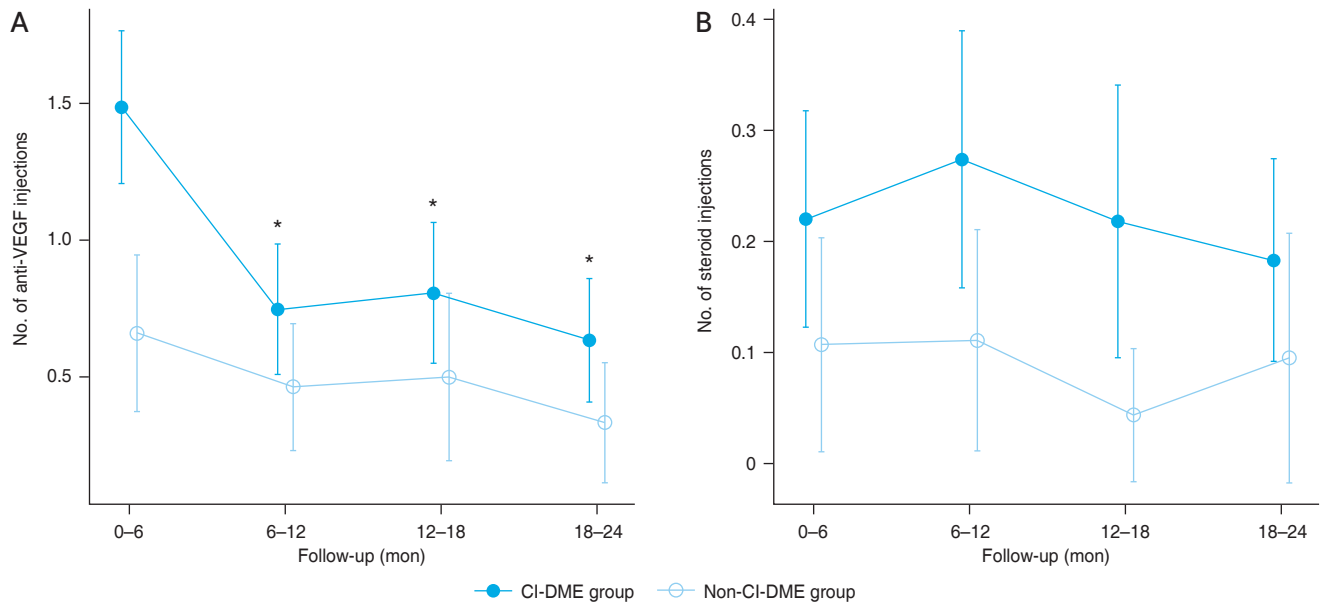


Fig. 5. Number of injections during the follow-up. (A) Anti-vascular endothelial growth factor (anti-VEGF) injections. (B) Steroid injections. CI-DME = center-involving diabetic macular edema. * $p < 0.05$.

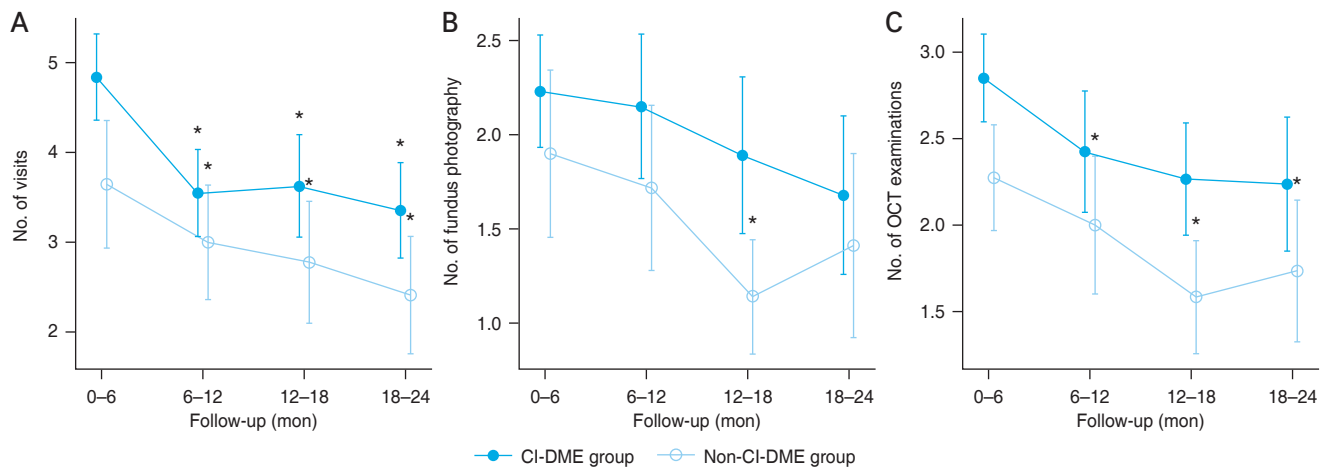


Fig. 6. Examinations during the follow-up. (A) Number of visits. (B) Number of fundus photography. (C) Number of optical coherence tomography (OCT) examinations. CI-DME = center-involving diabetic macular edema. * $p < 0.05$.

also showed no significant improvement in visual acuity, which may be attributed to undertreatment and the heterogeneity of the patient population.

Steroid injections were not frequently administered but were consistently used over the 2-year period (0.7 ± 1.5 times). This is more than a previous study in the United States (0.3 injections in the 24-month cohort) [10] but less frequent than in a Japanese study (2.0 ± 1.3 for 2 years) [20]. The use of local steroids is likely to vary depending on the healthcare environment of each country, such as accessibility to cataract surgery.

Over the 24-month period, patients visited an average of 14.2 times, equating to more than every other month. OCT was performed approximately nine times, roughly every 2 to 3 months. While this frequency is lower than the monthly visits and examinations seen in clinical trials, it is relatively reasonable considering the nature of real-world data. However, we found that the number of visits and OCT examinations decreased over 2 years. In a previous study investigating DME treatment patterns and healthcare resource utilization in Korea, the number of clinical visits, treatment visits, and visits for OCT and fluorescein angi-

ography were highest in the first 6 months, followed by a decline by year 3 [23]. This suggests the need for measures to ensure continuous follow-up for DME patients.

This study has several limitations. The small sample size reduced the reliability of the statistical analysis. Additionally, incomplete follow-up, with not all baseline patients reaching visit 5, and missing data at intermediate visits further hindered the analysis. One of the major factors contributing to the high rate of follow-up loss in our study may be the large proportion of patients treated at tertiary referral hospitals, where limited accessibility due to economic, geographic, and time constraints is common. Furthermore, reduced adherence to regular intravitreal injections or examinations over time likely played a role. This trend has also been noted in previous studies, which reported a gradual decline in compliance among patients with DME, often leading to poorer visual outcomes [24,25]. Furthermore, patients underwent examinations and treatments based on the judgment of retinal specialists at each institution, rather than following a standardized treatment and examination protocol. Lastly, although subgroup analyses based on insurance status, treatment cost, and the type of anti-VEGF agent could potentially provide important insights, these analyses were not feasible due to the lack of collected data or the heterogeneity of treatment patterns. Despite these limitations, this study remains valuable as it prospectively collected data from multiple South Korean medical institutions, providing insight into overall treatment and examination patterns for South Korean patients with DME.

In conclusion, DME patients recruited from multiple centers in South Korea showed poor visual outcome despite anatomical gains, likely due to the low number of injections. Encouraging continuous follow-up and treatment adherence in DME patients may help improve visual outcomes.

Conflicts of Interest: None.

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Supplementary Materials

Supplementary Fig. 1. Inclusion and exclusion criteria.

Supplementary Table 1. Number of treatments during the follow-up

Supplementary Table 2. Number of visits and ophthalmic examinations during the follow-up

Supplementary materials are available from <https://doi.org/10.3341/kjo.2025.0057>.

References

1. Im JH, Jin YP, Chow R, et al. Prevalence of diabetic macular edema based on optical coherence tomography in people with diabetes: a systematic review and meta-analysis. *Surv Ophthalmol* 2022;67:1244–51.
2. Yau JW, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care* 2012;35:556–64.
3. Teo ZL, Tham YC, Yu M, et al. Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. *Ophthalmology* 2021; 128:1580–91.
4. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. *N Engl J Med* 2015;372:1193–203.
5. Boyer DS, Yoon YH, Belfort R, et al. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. *Ophthalmology* 2014;121:1904–14.
6. Lee K, Chung H, Park Y, et al. Efficacy of intravitreal anti-vascular endothelial growth factor or steroid injection in diabetic macular edema according to fluid turbidity in optical coherence tomography. *Korean J Ophthalmol* 2014;28: 298–305.
7. Lee HY, Lee SY, Park JS. Comparison of photocoagulation with combined intravitreal triamcinolone for diabetic macular edema. *Korean J Ophthalmol* 2009;23:153–8.
8. Kim MS, Park SJ, Joo K, et al. Trends and barriers in diabetic retinopathy screening: Korea National Health and Nutritional Examination Survey 2016–2021. *J Korean Med Sci* 2024;39:e203.
9. Yoon K, Kim ES, Yu SY, et al. Clinical characteristics and long-term outcomes in diabetic macular edema patients: with or without additional injection following ranibizumab

- loading. *Korean J Ophthalmol* 2022;36:398–406.
10. Ciulla TA, Bracha P, Pollack J, et al. Real-world outcomes of anti-vascular endothelial growth factor therapy in diabetic macular edema in the United States. *Ophthalmol Retina* 2018;2:1179–87.
11. Gonder JR, Walker VM, Barbeau M, et al. Costs and quality of life in diabetic macular edema: Canadian burden of diabetic macular edema observational study (C-REALITY). *J Ophthalmol* 2014;2014:939315.
12. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema: two-year results from a comparative effectiveness randomized clinical trial. *Ophthalmology* 2016;123:1351–9.
13. Heier JS, Korobelnik JF, Brown DM, et al. Intravitreal aflibercept for diabetic macular edema: 148-week results from the VISTA and VIVID studies. *Ophthalmology* 2016;123:2376–85.
14. Ciulla TA, Pollack JS, Williams DF. Visual acuity outcomes and anti-VEGF therapy intensity in diabetic macular oedema: a real-world analysis of 28 658 patient eyes. *Br J Ophthalmol* 2021;105:216–21.
15. Kuo BL, Tabano D, Garmo V, et al. Long-term treatment patterns for diabetic macular edema: up to 6-year follow-up in the IRIS® registry. *Ophthalmol Retina* 2024;8:1074–82.
16. Durukan AH, Unlu N, Onen M, et al. Anti-vascular endothelial growth factor therapy in diabetic macular edema: real-life outcomes from a multicenter study in Turkey over 36 months. *Int Ophthalmol* 2022;42:3777–87.
17. Wong TY, Haskova Z, Asik K, et al. Faricimab treat-and-extend for diabetic macular edema: two-year results from the randomized phase 3 YOSEMITE and RHINE trials. *Ophthalmology* 2024;131:708–23.
18. Nguyen QD, Brown DM, Marcus DM, et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. *Ophthalmology* 2012;119:789–801.
19. Gabrielle PH, Nguyen V, Creuzot-Garcher C, et al. Three-year treatment outcomes of aflibercept versus ranibizumab for diabetic macular edema: data from the Fight Retinal Blindness! Registry. *Retina* 2022;42:1085–94.
20. Shimura M, Kitano S, Muramatsu D, et al. Real-world management of treatment-naïve diabetic macular oedema in Japan: two-year visual outcomes with and without anti-VEGF therapy in the STREAT-DME study. *Br J Ophthalmol* 2020;104:1209–15.
21. Cho H, Choi KS, Lee JY, et al. Healthcare resource use and costs of diabetic macular oedema for patients with anti-vascular endothelial growth factor versus a dexamethasone intravitreal implant in Korea: a population-based study. *BMJ Open* 2019;9:e030930.
22. Stewart MW. Treatment of diabetic retinopathy: recent advances and unresolved challenges. *World J Diabetes* 2016;7:333–41.
23. Park KH, Kim YY, Jo YJ, et al. Healthcare utilization and treatment patterns in diabetic macular edema in Korea: a retrospective chart review. *J Korean Med Sci* 2019;34:e118.
24. Weiss M, Sim DA, Herold T, et al. Compliance and adherence of patients with diabetic macular edema to intravitreal anti-vascular endothelial growth factor therapy in daily practice. *Retina* 2018;38:2293–300.
25. Kumar G, Velu S, Rajalakshmi R, et al. Compliance with follow-up in patients with diabetic macular edema: eye care center vs. diabetes care center. *Indian J Ophthalmol* 2023;71:2531–6.

Inclusion criteria	Exclusion criteria
- Adults aged 20 years or older with a diagnosis of type 1 or type 2 diabetes at the time of screening. - Presence of significant retinal thickening within the ETDRS grid circle (6 mm in diameter) in the study eye, as assessed by spectral-domain OCT. - Presence of focal or diffuse leakage in the macular area, as confirmed by fluorescein angiography. (1) CI-DME group - Retinal thickening within 500 μm of the foveal center, as observed on fundus examination, or the presence of hard exudates within 500 μm of the foveal center with adjacent retinal thickening. - CST of ≥ 300 μm within the 1 mm ETDRS central subfield on spectral-domain OCT. (2) Non-CI-DME group - Retinal thickening of at least one disc diameter located ≥ 500 μm away from the foveal center, as observed on fundus examination. - CST of ≤ 300 μm within the 1-mm ETDRS central subfield on spectral-domain OCT. - Retinal thickening of ≥ 400 μm located ≥ 500 μm away from the foveal center. If both eyes meet the criteria for DME, only one eye will be included based on the following criteria: - If one eye has CI-DME and the other has non-CI-DME, the non-CI-DME eye will be included in the non-CI-DME group. - If both eyes have CI-DME or both have non-CI-DME, the eye with the better BCVA will be selected for inclusion in the respective group.	- Clinically suspected pseudophakic cystoid macular edema. - History of vitreoretinal surgery, scleral buckling, panretinal photocoagulation, cataract surgery, prior intraocular or periocular corticosteroid use, focal laser or photodynamic therapy for macular disease in the study eye, or anti-VEGF treatment in either eye within the past 3 months. - Presence of active proliferative diabetic retinopathy, history of uveitis, aphakia, or any condition affecting central vision, including vitreomacular traction or epiretinal membrane, as confirmed by biomicroscopy or OCT. Additionally, presence of iris neovascularization, vitreous hemorrhage, tractional retinal detachment, retinal pigment epithelial atrophy, subretinal fibrosis or scarring, or any structural macular damage that may prevent visual improvement following treatment. Evidence of infectious blepharitis, keratitis, or scleritis in either eye, or any concomitant ocular condition other than DME that may impair vision, require medical or surgical intervention during the study period, or interfere with study outcome interpretation (e.g., retinal vein occlusion, retinal detachment, macular hole, or choroidal neovascularization). - History of glaucoma filtration surgery in the study eye, intraocular pressure ≥ 25 mmHg, high myopia with spherical equivalent < -8.00 D or axial length > 26 mm, or presence of media opacities that interfere with fundus and OCT imaging. - Ongoing treatment for a severe systemic infection. - History of systemic anti-VEGF therapy within the past 6 months or a history of stroke and/or myocardial infarction. - Pregnancy or breastfeeding. - Known allergy to fluorescein dye.

Supplementary Fig. 1. Inclusion and exclusion criteria. ETDRS = Early Treatment of Diabetic Retinopathy Study; OCT = optical coherence tomography; CI-DME = center-involving diabetic macular edema; CST = central subfield thickness; BCVA = best-corrected visual acuity; VEGF = vascular endothelial growth factor; DME = diabetic macular edema; D = diopters.

Supplementary Table 1. Number of treatments during the follow-up

Treatment	Follow-up (mon)			
	0–6	6–12	12–18	18–24
Anti-VEGF injection				
CI-DME group	1.5 ± 1.5	0.7 ± 1.2	0.8 ± 1.2	0.6 ± 1.0
Non-CI-DME group	0.7 ± 1.1	0.5 ± 0.9	0.5 ± 1.0	0.3 ± 0.7
Total	1.2 ± 1.4	0.6 ± 1.1	0.7 ± 1.1	0.5 ± 0.9
Steroid injection				
CI-DME group	0.2 ± 0.5	0.3 ± 0.6	0.2 ± 0.6	0.2 ± 0.4
Non-CI-DME group	0.1 ± 0.4	0.1 ± 0.4	0 ± 0.2	0.1 ± 0.4
Total	0.2 ± 0.5	0.2 ± 0.5	0.2 ± 0.5	0.2 ± 0.4
Focal laser				
CI-DME group	0 ± 0.1	0 ± 0	0 ± 0.2	0 ± 0.2
Non-CI-DME group	0.2 ± 0.4	0.1 ± 0.2	0.1 ± 0.2	0 ± 0
Total	0.1 ± 0.3	0 ± 0.1	0 ± 0.2	0 ± 0.1
Panretinal photocoagulation				
CI-DME	0.3 ± 0.8	0.1 ± 0.5	0.1 ± 0.4	0 ± 0.3
Non-CI-DME	0.2 ± 0.5	0.1 ± 0.4	0.2 ± 0.6	0.1 ± 0.4
Total	0.3 ± 0.7	0.1 ± 0.5	0.1 ± 0.5	0.1 ± 0.3

Values are presented as mean ± standard deviation.

VEGF = vascular endothelial growth factor; CI-DME = center-involving diabetic macular edema.

Supplementary Table 2. Number of visits and ophthalmic examinations during the follow-up

Variable	Follow-up (mon)			
	0–6	6–12	12–18	18–24
No. of visits				
CI-DME group	4.8 ± 2.5	3.5 ± 2.4	3.6 ± 2.6	3.4 ± 2.5
Non-CI-DME group	3.6 ± 2.7	3.0 ± 2.4	2.8 ± 2.4	2.4 ± 2.2
Total	4.4 ± 2.7	3.4 ± 2.4	3.3 ± 2.5	3.0 ± 2.4
Fundus photography				
CI-DME group	2.2 ± 1.6	2.1 ± 1.9	1.9 ± 1.9	1.7 ± 1.9
Non-CI-DME group	1.9 ± 1.7	1.7 ± 1.6	1.1 ± 1.0	1.4 ± 1.6
Total	2.1 ± 1.6	2.0 ± 1.8	1.6 ± 1.7	1.6 ± 1.8
OCT examination				
CI-DME group	2.9 ± 1.4	2.4 ± 1.7	2.3 ± 1.5	2.2 ± 1.8
Non-CI-DME group	2.3 ± 1.2	2.0 ± 1.5	1.6 ± 1.1	1.7 ± 1.4
Total	2.7 ± 1.3	2.3 ± 1.7	2.0 ± 1.4	2.1 ± 1.7
Fluorescein angiography				
CI-DME group	0.1 ± 0.3	0.2 ± 0.5	0 ± 0.2	0.1 ± 0.2
Non-CI-DME group	0 ± 0.1	0 ± 0.2	0.1 ± 0.3	0.1 ± 0.4
Total	0.1 ± 0.3	0.2 ± 0.4	0.1 ± 0.3	0.1 ± 0.3

Values are presented as mean ± standard deviation.

CI-DME = center-involving diabetic macular edema; OCT = optical coherence tomography.