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EDITORIAL

How to manage patients with center-involving diabetic macular edema and good visual acuity? An answer to a common clinical question

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The recent publication of "Effect of Initial Management with Aflibercept vs Laser Photocoagulation vs Observation on Vision Loss Among Patients with Diabetic Macular Edema Involving the Center of the Macula and Good Visual Acuity" by Baker et al. [1] provides valuable clinical insight into a common clinical question frequently encountered by general ophthalmologists as well as retina specialists. Diabetic macular edema (DME) is the most common cause of vision loss in diabetic patients, and constitutes a very commonly encountered ocular pathology [2, 3]. The RISE and RIDE studies have demonstrated that intravitreal injections of antiendothelial vascular growth factor (VEGF) agents are a safe and effective therapy for DME [4], and since then multiple additional randomized controlled trials (RCTs) have established them as the first-line treatment for this condition, and their superiority over laser treatment [5]. These RCTs included patients with DME and a best-corrected visual acuity (VA) of 20/32 or worse. However, patients with center-involving DME with better VA are very common, and no there is no consensus regarding their optimal management strategy as such cases were not included in the major RCTs. Should these patients be observed, or is early intervention needed in order to prevent deterioration? And if so, what treatment should be recommended?

The Diabetic Retinopathy Research Network has designed the "Protocol V" RCT in order to address this common and important clinical question. This multicenter RCT included 702 eyes of patients with center-involving DME and a VA of 20/25 or better. This unique cohort was randomly divided into a 1:1:1 manner to treatment with intravitreal aflibercept, macular laser or observation, and followed for 2 years. The primary outcome measure was a decrease of five letters in VA compared with baseline, which was deemed as a clinically significant change in these patients. Following the first injection, eyes in the aflibercept group were followed monthly and the need for additional injections was assessed on every visit. If injections were deferred on three consecutive visits (after the first six visits), the follow-up interval was extended to 8–16 weeks, compatible with the clinical reality. Eyes treated by laser or observation were followed after 8 weeks and every 16 weeks thereafter, and could receive aflibercept injections if worsening occurred.

The median number of injections in the aflibercept group was 8 (range 6–11) after 2 years of follow up. This is a relatively low rate of injections compared with that reported in previous studies on DME with worse VA [4, 5]. In the laser group, aflibercept injections were administered in 25% of the cases, and in 40% of the cases in the observation group. Rates of at least a five letter loss in VA were 16% in the aflibercept group, 17% in the laser group, and 19% in the observation group, with no significant difference between groups. Mean change in final VA compared with baseline was 0.9 ± 6.4 letters in the aflibercept group, 0.1 ± 6.3 letters in the laser group and -0.4 ± 6.4 letters in the observation group, also without significant difference between groups. Rates of final VA of 20/20 or better were 77% in the aflibercept group, 71% in the laser group, and 66% in the observation group. A statistically significant difference was noted for this secondary outcome measure between aflibercept and observation ($p = 0.03$). There was no significant difference between groups regarding change in retinal thickness. The safety profile was excellent in all three groups, with the only difference being a higher rate of

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intraocular pressure elevation in the aflibercept group (8%, compared with 6% with laser and 3% with observation).

This is an important study as its results are the first to provide level 1 evidence on the optimal treatment strategy for patients with central DME and good VA. It is a relatively large study with a very homogenous cohort, and compared the three possible treatment options available for these patients. Given the excellent baseline at presentation, the results achieved in the aflibercept group can represent those achieved with any anti-VEGF agent. The treatment and monitoring protocols were compatible with the real-world practice, with a very high completion rate in all groups. In all three groups—aflibercept, laser, and observation—mean final VA was 20/20 and changes in VA and retinal thickness were not significantly different. The proportion of eyes with final VA of 20/20 was greater in the aflibercept group than in the observation group, and deterioration that required aflibercept treatment occurred in 25% of eyes in the laser group and 40% of eyes in the observation group. In addition, it should be conditioned that intravitreal injections are associated with significant costs, as well as risk (although small) of endophthalmitis and other adverse events.

In conclusion, the results of this study indicate that in patients with central DME and good VA acuity, observation is an appropriate treatment strategy, which will result in most cases in maintenance of good VA without increasing cost or risk. Observation should of course include timely monitoring, to detect any changes early and initiate anti-VEGF treatment if necessary, in order to preserve good VA with relatively fewer injections than generally required for patients with DME and worse VA. In the future, telemedicine and home monitoring may become part of the monitoring strategy for these patients. It will allow them to be monitored as frequently as needed while reducing the burden on the clinics, and enable early detection of patients whose observation should be replaced with treatment.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Baker CW, Glassman AR, Beaulieu WT, Antoszyk AN, Browning DJ, Chalam KV, DRCR Retina Network. et al. Effect of initial management with aflibercept vs laser photocoagulation vs observation on vision loss among patients with diabetic macular edema involving the center of the macula and good visual acuity: a randomized clinical trial. J Am Med Assoc. 2019;321:1880–94.
2. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis. 2015;2:17.
3. Das A, McGuire PG, Rangasamy S. Diabetic macular edema: pathophysiology and novel therapeutic targets. Ophthalmology. 2015;122:1375–94.
4. Nguyen QD, Brown DM, Marcus DM, Boyer DS, Patel S, Feiner L, RISE and RIDE Research Group. et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. Ophthalmology. 2012;119:789–801.
5. Diabetic Retinopathy Clinical Research Network, Elman MJ, Aiello LP, Beck RW, Bressler NM, Bressler SB, Edwards AR, et al. Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. Ophthalmology 2010;117:1064–77.