

## The Nonadherent Patient with Diabetic Macular Edema

*David J. Browning MD, PhD*

### Brief summary of the literature

Vitreotomy for diabetic macular edema was first reported by Lewis and colleagues in 1992.<sup>1</sup> They applied the method to patients with taut, adherent vitreous to the macula. Subsequently, it was applied to patients without discernible vitreomacular traction.<sup>2</sup> In both groups of patients the technique reproducibly leads to macular thinning, but the visual acuity outcomes have not been consistent.

The study with highest methodologic quality to date regarding the technique was the DRCR network protocol D, which was reported in 2010.<sup>3</sup> In the primary cohort of 87 patients with vitrectomy and vitreomacular traction based on clinical examination, the baseline median best corrected visual acuity was 20/100 and median macular thickness was 491  $\mu\text{m}$ . At the primary outcome visit at 6 months, the median visual acuity remained 20/100, but the median macular thickness change was -160  $\mu\text{m}$ . However, this study has been criticized because the eyes enrolled had a history of many previous treatments for diabetic macular edema (44% had previous focal laser and 30% had previous intravitreal steroid injection) and yet had refractory edema, leading to the suspicion that their maculas were unable to respond as well as if they had received vitrectomy earlier in the course of DME. Moreover, the study was unable to separate the effects of cataract which were present in 43% percent of eyes, and which presumably advanced after vitrectomy and partially nullified any visual acuity benefits that would have been otherwise manifested.<sup>3</sup>

The advantages of vitrectomy for diabetic macular edema are that it is more durable and less expensive than anti-VEGF therapy. The disadvantages are that it is more invasive with possibly higher risk and it causes progression of cataract in phakic eyes. Vitrectomy for DME is common in Japan, Egypt, Poland, Mexico, China and many other countries with fewer financial resources for protracted regimens of intravitreal injections.<sup>4</sup> I use the method for my patients with more severe DME and no insurance (e.g., undocumented guest workers, who frequently have advanced diabetic retinopathy, severe diabetic macular edema, and no ability or money to adhere to a burdensome schedule of injections).<sup>5</sup>

### Issues raised by the case

1. The patient gave up on anti-VEGF therapy and switched doctors. How should the second physician respond?

*The fact that the patient gave up does not mean the treatment was not working. It may well have been working, but the patient could not appreciate the improvement or was expecting more or faster improvement. Whatever the reason, from the patient's perspective it was not working, and in the choice of a treatment, if the patient is not adherent, even an effective therapy will not work. The importance of communication and encouragement is highlighted by this common scenario. Showing the patient the OCT over time is a useful tool that can allay impatience and loss of will.*

2. The second line therapy (an intravitreal dexamethasone implant) that was suggested was also an injectational therapy. Failure to follow-up rendered the question of its effectiveness moot.

*The initial inference – that she had lost faith in one form of injectational treatment – was evidently not the case. She defaulted on following advice for any kind of injectational therapy. Vitrectomy was in this case a third line therapy which was arrived at by a series of patient “votes with her feet”. One might take the approach that nonadherence to a treatment recommendation should imply discharging the patient*

*from one's practice, but there are too many nonadherent diabetic patients to make this approach feasible.*

3. What exactly is involved in a vitrectomy approach?

*At the minimum the approach involves vitrectomy with induced separation of the posterior hyaloid from the macula. This leads to increased vitreal oxygen and downregulation of VEGF.<sup>6</sup> Some surgeons add focal laser, panretinal laser, or both. Some surgeons peel the internal limiting membrane (ILM). Some surgeons add triamcinolone or a dexamethasone implant at the end of the procedure. There is no evidence that any particular step adds value.<sup>7</sup> My thinking on the matter is to provide a maximalist approach, covering all possible contributing factors to the DME, because the patient has demonstrated repeated nonadherence, I may not get the opportunity to see her again, and I would like to protect her from the future adverse effects of her behavior. In these cases, my discussion with the patient makes explicit the driving influence of nonadherence on treatment recommendations. I have not seen denial and pushback from patients.*

#### Reference List

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2. Otani T, Kishi S. A controlled study of vitrectomy for diabetic macular edema. *Am J Ophthalmol* 2002;134:214-9.
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4. Landers MB III, Kon Graverson VA, Stewart MW. Early vitrectomy for DME; Does it have a role? *Retinal Physician* 2013;10:46-53.
5. Browning DJ, Lee C, Stewart MW, Landers III MB. Vitrectomy for center-involved diabetic macular edema. *Clinical Ophthalmology* 2016;10:735-42.
6. Holekamp NM, Shui YB, Beebe DC. Vitrectomy surgery increases oxygen exposure to the lens: a possible mechanism for nuclear cataract formation. *Am J Ophthalmol* 2005;139:302-10.
7. Browning DJ. Diabetic macular edema. In: Browning DJ, ed. **Diabetic retinopathy, Evidence-based management**, first ed. New York: Springer Inc, 2010; chap. 7.

Slide 1

**The Nonadherent Patient with  
Diabetic Macular Edema**

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Slide 2

**75 year old woman with longstanding blurry vision OU and type 2 DM, hypertension, hypercholesterolemia, and 2 previous strokes**

- 1/4/2018
  - Had previously seen another retina specialist and was given anti-VEGF injections OU which she abandoned "because they weren't working"
  - VA R- CF 5 ft, L – 20/80
  - IOP 12 OU
  - PCIOL OU

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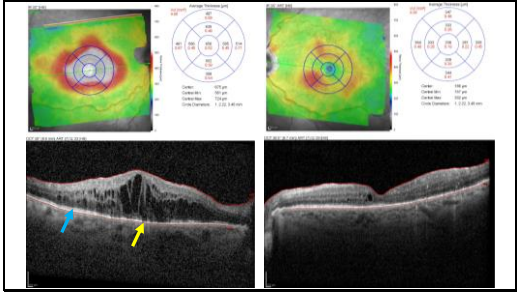
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Slide 3




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Slide 4

**1/4/2018**

- Notice no IVFA – use has decreased in past 10 years with SD-OCT and lack of impact on decision making and prognosis
  - Prognosis can be adequately assessed from history, exam, and SD-OCT
  - DRIL (disorganization of the retinal inner layers)
  - EZ (ellipsoid zone) status

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Slide 5

What would you recommend?

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Slide 6

- Because of documented nonadherence to anti-VEGF, I recommended intravitreal dexamethasone implant

**Failure to follow-up**

- 1/3/2019
  - VA R-20/400, L-20/100

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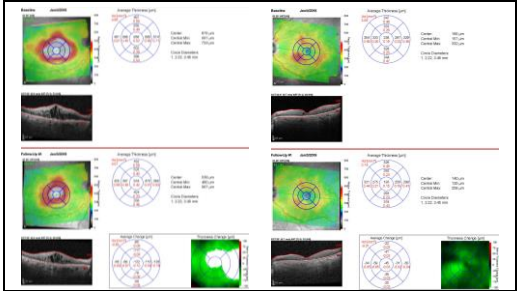
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Slide 7



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Slide 8

- Note significant spontaneous fluctuation in CST
- Note fluctuation in subclinical DME OS
- In view of nonadherence with all forms of office therapy, I recommended VTX/ILM peel/ focal and PRP laser/intravitreal triamcinolone
- Returned 2/14/2019
  - VA R-20/400, L-20/80

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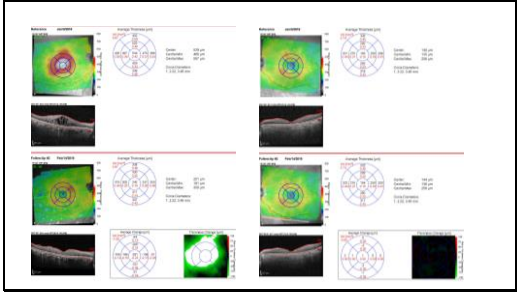
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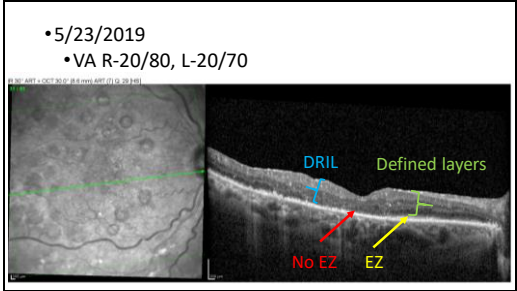
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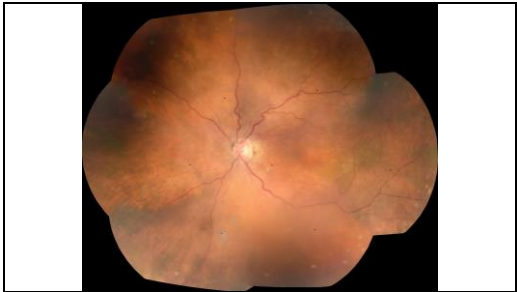
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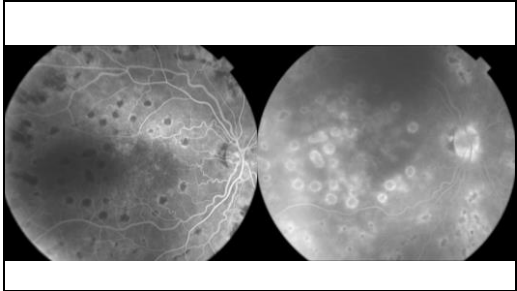
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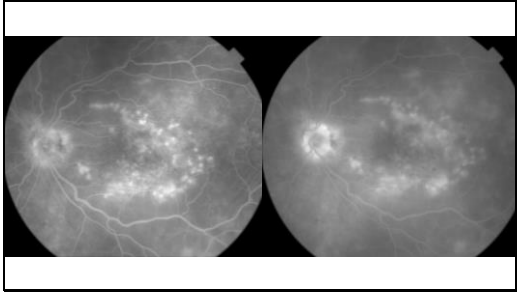
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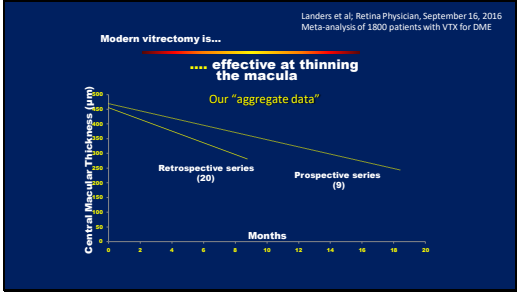
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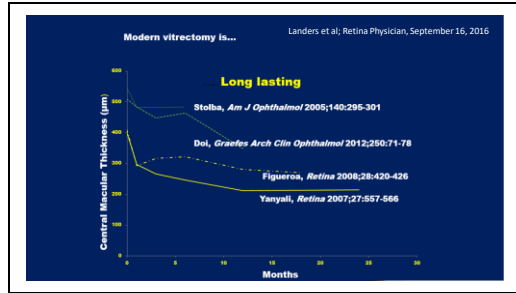
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Slide 17

Clinical Ophthalmology Dovepress  
ORIGINAL RESEARCH

### Vitrectomy for center-involved diabetic macular edema

This article was published in the following Dove Press journal  
Clinical Ophthalmology  
26 April 2016  
Number of times this article has been viewed

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**Purpose:** To determine the effect of vitrectomy for center-involved diabetic macular edema (CI-DME).

**Methods:** This was a retrospective study of 45 patients who had vitrectomy for CI-DME and were followed up for at least 12 months. Charts were reviewed for visual acuity (VA), central subfield mean thickness measured by optical coherence tomography, prerogical and postretrol interventions for CI-DME, and number of office visits in the first 12 months after surgery. Preoperative spectral domain optical coherence tomography was performed on 38 patients, and they were graded for ellipsoid zone (EZ) intactness by three independent graders with assessment of agreement between graders using intraclass correlation coefficients.

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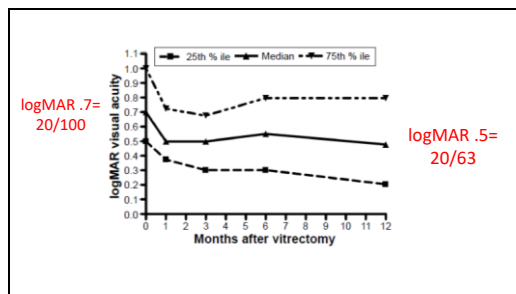
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Slide 19

**Assessing Nonadherence is Important in Developing a Treatment Plan**

- How long since the patient has seen an eye doctor?
- How long since the patient has seen a PCP/ endocrinologist?
- A1C?
- Insurance status – underinsured implies nonadherence

• When a patient is judged nonadherent, generally choose more durable treatments, even if higher risk and less effective

- Focal rather than anti-VEGF
- PRP rather than anti-VEGF
- Vitrectomy approaches

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Slide 20

Discussion, Questions, and Comments

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