

# EFFECT OF DRIL (DISORGANIZATION OF THE RETINAL INNER LAYERS) ON VISUAL ACUITY OF DIABETIC MACULAR EDEMA PATIENTS ON STANDARD TREATMENT WITH ANTI-VASCULAR ENDOTHELIAL GROWTH FACTORS

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## Abstract

**Objective:** To study the effect of DRIL on visual acuity of diabetic macular edema patients on standard treatment with Anti-Vascular Endothelial Growth Factors in terms of mean change in Best-Corrected Visual Acuity after treatment of DRIL.

**Methods:** In this study, we included 66 patients with a diagnosis of DRIL due to DME having aged 18-70 years. The study was conducted from 31 July 2024 to 30 January 2025. The assessment of Best-Corrected Visual Acuity (BCVA) for each participant was conducted by the researcher using Snellen's Chart. Following the initial treatment, patients received an intravitreal injection of Bevacizumab at a dose of 1.25 mg. A month later, a follow-up assessment was conducted to evaluate the changes in best-corrected visual acuity (BCVA). Additionally, the presence of disruption of the inner retinal layers (DRIL) was assessed using optical coherence tomography (OCT). All findings were systematically documented.

**Results:** The average age of participants was found to be  $58.7 \pm 8.9$  years. Among the 66 participants, 35 individuals, accounting for 53%, were male. At baseline, the Best Corrected Visual Acuity (BCVA) was measured at  $0.68 \pm 0.31$ . After one month, the BCVA was observed to be  $0.55 \pm 0.28$ . This resulted in a mean change in BCVA of  $0.13 \pm 0.29$ , indicating a notable shift in visual acuity over the observed period.

**Conclusion:** Treatment of DRIL is associated with significant improvements in BCVA in diabetic macular edema (DME) patients. All patients of DME with reduced vision should be evaluated for the presence of DRIL, as treating the DRIL can improve visual acuity in these patients.

## INTRODUCTION

Diabetes mellitus (DM) poses a significant health challenge for individuals of working age. It is estimated that around 93 million people worldwide are suffering from diabetic retinopathy (DR).<sup>1</sup> A major

consequence of DR is diabetic macular edema (DMO), which is the primary cause of vision impairment among those with diabetic retinopathy, impacting roughly 7% of individuals with DM.<sup>2</sup> In

2021, approximately 536.6 million people were living with diabetes globally, and projections indicate that this figure could rise to 783.2 million by 2045.<sup>3</sup> Diabetic Macular Edema (DME) is characterized by an accumulation of fluid within the central retina, and it plays a major role in causing vision impairment. Studies using fundus photography have shown a noticeable decline in visual acuity (VA) as diabetic retinopathy (DR) progresses in patients suffering from DME.<sup>4</sup> Optical Coherence Tomography (OCT) has become the preferred method for detecting changes in the retinal structure and assessing the extent of retinal thickening due to DME. Remarkably, in cases of moderate DME, high-resolution OCT can reveal subtle retinal thickness that may not be apparent during standard clinical evaluations.<sup>5, 6</sup> One significant finding in this context is the Disorganization of Retinal Inner Layers (DRIL), an OCT-based biomarker that has been associated with predicting both baseline and post-macular edema visual outcomes in patients with DM.<sup>7</sup>

Disorganization of the inner retinal layers that affects 50% or more of the central 1-mm zone around the fovea, known as foveal DRIL, is linked to poorer visual acuity (VA). This correlation remains significant even in cases where vision is diminished despite the resolution of edema. Conversely, it can also apply to situations where good vision is observed despite the presence of ongoing edema. The strong relationship between foveal DRIL and visual acuity highlighted in a previous cross-sectional study underscores the need for further longitudinal research to explore foveal DRIL as a potential predictor of future visual acuity in patients with current DME.<sup>8</sup>

The aim of this study was to study the effect of DRIL on visual acuity of diabetic macular edema patients on standard treatment with Anti-Vascular Endothelial Growth Factors in terms of mean change in Best-Corrected Visual Acuity after treatment of DRIL.

## METHODS:

In this study, we included 66 patients with a diagnosis of DRIL due to DME having aged 18-70 years. The study was conducted from 31 July 2024 to 30 January 2025. While patients with considerable cataracts, corneal degeneration, and opacity, a history of intravitreal treatments or vitreous surgery, as well as those suffering from other eye conditions that can

lead to macular edema—such as uveitis, retinal vein occlusion, or choroidal neovascularization were excluded.

Participants who met the inclusion criteria were invited to join the study after a comprehensive explanation of its objectives and procedures, followed by the acquisition of written informed consent. Once consent was obtained, baseline demographic and clinical data, including age, gender, place of residence, and duration of symptoms, were recorded using a standardized form. The assessment of Best-Corrected Visual Acuity (BCVA) for each participant was conducted by the researcher using Snellen's Chart. Each patient underwent a thorough examination that included slit-lamp analysis and dilated fundus evaluation. If there was a suspicion of Dismissal of Retinal Integrity Loss (DRIL), confirmation was obtained through Optical Coherence Tomography (OCT) using the NiDEKRS-330 software (NAVIS EX 1.5.2.0) in line with the established operational definitions. Tomographic images were taken from both eyes with horizontal and vertical scans through the fovea, followed by a 6 × 6 mm macular raster scan. Additionally, color photographs were captured subsequent to pupillary dilation. The acquired images were analyzed thoroughly using proprietary software, where all B-scans from the 6 × 6 macular raster were reviewed to document the presence or absence of DRIL.

Following the initial treatment, patients received an intravitreal injection of Bevacizumab at a dose of 1.25 mg. A month later, a follow-up assessment was conducted to evaluate the changes in best-corrected visual acuity (BCVA). Additionally, the presence of disruption of the inner retinal layers (DRIL) was assessed using optical coherence tomography (OCT). All findings were systematically documented, and a comparative analysis was performed to determine the correlation between the presence or absence of DRIL and the corresponding BCVA values.

Data was analyzed using SPSS v25. Mean change in BVCA was presented using mean and SD.

## RESULTS:

In a recent study, the average age of participants was found to be 58.7±8.9 years. Among the participants, 35 individuals, accounting for 53%, were male. Additionally, the average duration of diabetes among

the participants was 19.4 years, with a standard deviation of 10.3 years.

The study outcomes are summarized in Table 2. At baseline, the Best Corrected Visual Acuity (BCVA) was measured at  $0.68 \pm 0.31$ . After one month, the BCVA was observed to be  $0.55 \pm 0.28$ . This resulted in a mean change in BCVA of  $0.13 \pm 0.29$ , indicating a notable shift in visual acuity over the observed period (Table 2).

**Table 1. Baseline Characteristics.**

Age	58.7±8.9
Male Gender	35 (53%)
Diabetes Duration (Years)	19.4±10.3

**Table 2. Study Outcomes.**

Baseline BCVA	0.68±0.31
BCVA at one Month	0.55±0.28
Mean change in BCVA	0.13±0.29

## DISCUSSION:

Disruption of the retinal inner layers (DRIL) is a frequently observed response to retinal stress, manifesting in various retinal disorders. These conditions include retinal vein occlusion (both central and branch types), central retinal artery occlusion, diabetic retinopathy, uveitis (which involves inflammation of the uvea), retinitis pigmentosa (a collection of inherited retinal disorders), epiretinal membranes (transparent layers that can form on the retina's surface), and closed globe trauma (eye injury without rupture).<sup>9-12</sup> Despite the wide range of conditions associated with DRIL, the precise mechanisms behind its emergence—especially concerning uveitic macular edema (UME)—and its impact on best-corrected visual acuity (BCVA) remain poorly understood. Two significant factors are believed to play a crucial role in the development of DRIL in the context of UME: inflammation and ischemia (insufficient blood flow). Inflammation represents a natural immune response, but in cases like uveitis, it can become chronic and detrimental, affecting the fragile structures within the retina. Ischemia deprives retinal cells of essential oxygen and nutrients, resulting in cellular dysfunction and damage. A pivotal study by Nicholson et al.<sup>12</sup> found a strong association between DRIL and retinal capillary nonperfusion as revealed by fundus fluorescein

angiography. This evidence highlights the importance of vascular compromise and resulting ischemia in the onset of DRIL. The retina's complex cellular architecture is vital for proper visual function, with bipolar cells playing a central role in this network. These cells act as the exclusive communication link between photoreceptors (the cells that detect light) and ganglion cells (which relay visual information to the brain). Therefore, any damage or disruption to bipolar cells can significantly affect visual acuity. Sun et al. suggests that DRIL directly undermines this critical communication pathway, disrupting the efficient transmission of visual signals from photoreceptors to ganglion cells.<sup>13</sup> Research has indicated a direct correlation between the severity of DRIL and the extent of damage to bipolar cell axons. As DRIL advances, these axons, responsible for relaying electrical impulses, may become overstretched and can potentially rupture in severe instances.<sup>14</sup> Retinal cells, like other biological tissues, possess a certain level of elasticity that allows them to accommodate some degree of stretching. However, when the swelling or stress that induces DRIL surpasses this elastic threshold, it can lead to a disruptive effect on the delicate neuronal axons, impairing signal transmission. This concept provides a plausible explanation for the strong link observed between DRIL and diminished visual acuity.<sup>15</sup> Specifically, studies have illustrated that the extent of DRIL is a key parameter closely associated with poorer BCVA outcomes. This suggests that prolonged and excessive stretching of bipolar axons, ultimately causing their injury or loss, is a major factor in the decline of visual function in affected patients. Further investigations are necessary to unravel the complex mechanisms that drive DRIL and to develop effective approaches to prevent its progression and protect vision.

Liu et al. studied the role of DRIL as predictor of visual acuity in macular edema secondary to uveitis and reported that a greater DRIL range at baseline (Transverse diameter  $684.07 \pm 267.51 \mu\text{m}$ , Vertical Diameter  $267.07 \pm 104.61 \mu\text{m}$ ) was associated with worse baseline BCVA ( $0.55 \pm 0.23 \log\text{MAR}$ ).<sup>16</sup>

In present study, we find significant improvement in BCVA after DRIL treatment using VEGF factor in eyes with DME. After one month of treatment, mean change in BCVA was  $0.13 \pm 0.29 \log\text{MAR}$ .

Eraslan et al, also studied relationship between DRIL and Final Visual Acuity Score in Diabetic macular edema patients. 10.1% patients with diabetic macular edema had findings of DRIL. BCVA before and after intravitreal injection of ranibizumab was  $0.3 \pm 0.22$  and  $0.36 \pm 0.26$  respectively.<sup>17</sup> Similar results were reported by Minh et al. who reported significant improvement in BCVA after the resolution of DRIL in patients of retinal vein occlusion patients. Moreover the authors reported that all Anti-VEGF agents are equally effective in resolution of DRIL.<sup>18</sup> This research has certain limitations due to its sample size. To gain a clearer understanding of the connection between DRIL and vision in patients with DME, more extensive prospective studies, particularly clinical trials, would be beneficial. Such studies would allow for a detailed evaluation of the impact that various anti-VEGF agents have on DRIL in DME patients over the long term. Additionally, the absence of a control group complicates the ability to determine if the observed improvements in DRIL levels among most patients can be attributed directly to the use of anti-VEGF agents.

## CONCLUSION:

Treatment of DRIL is associated with significant improvements in BCVA in diabetic macular edema (DME) patients. All patients of DME with reduced vision should be evaluated for the presence of DRIL, as treating the DRIL can improve visual acuity in these patients.

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