SOMATO PUBLICATIONS ISSN: XXXX-XXXX

Annals of Ophthalmology and Eye Disorders

Review Article

Predictors of visual acuity improvement in diabetic patients with retinal disease with corneal ulcer

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Received: 28 July 2022; Accepted: 26 October 2022; Published: 17 January 2023.

Citation of this article: Ricci M, Romano S, Bruno M (2023) Predictors of visual acuity improvement in diabetic patients with retinal disease with corneal ulcer. Ann Ophthalmol Eye Disord, 5(1): 01-06. DOI: 10.5281/zenodo.22812190

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Abstract

Background: Diabetic patients whose eyes carry both retinal disease and a corneal ulcer present a prognostic challenge, because an unstable corneal surface degrades measured acuity and constrains treatment tempo, while the systemic factors that predict poor corneal healing also predict a blunted retinal treatment response.

Objective: This review synthesizes evidence on predictors of visual acuity improvement in diabetic patients with retinal disease complicated by corneal ulcer, drawing on the retinal treatment-response literature and the corneal healing literature together.

Methods: We reviewed randomized trials and cohort studies of anti-VEGF and laser therapy for diabetic macular edema and proliferative diabetic retinopathy, alongside clinical and mechanistic studies of corneal ulcer risk and healing in diabetes, synthesizing the two literatures given the scarcity of studies enrolling patients with both diagnoses concurrently.

Findings: Baseline visual acuity, macular edema chronicity and structural integrity, and macular ischemia remain the dominant predictors of retinal treatment response; diabetes duration, glycemic control, and corneal sensory neuropathy predict corneal ulcer occurrence and healing speed; and an active ulcer functions as a modifier that transiently degrades measured acuity, delays retinal treatment scheduling, and marks a patient whose overall disease severity already limits the retinal treatment ceiling.

Conclusions: Prompt recognition and management of the corneal component allows retinal treatment to proceed on schedule and clarifies the eye's true visual potential once the surface stabilizes; routine ocular surface screening is warranted in diabetic patients with long disease duration, poor glycemic control, and advanced retinopathy.

Keywords: diabetic retinopathy; corneal ulcer; visual acuity; diabetic keratopathy; macular edema

1. Introduction

Diabetic eye disease rarely stays confined to one tissue. A patient followed long enough in a diabetes clinic will often accumulate damage at more than one level of the visual axis: a retina thickened by macular edema or scarred by proliferative disease, and a cornea whose epithelium heals slowly, whose nerves have lost sensation, and whose surface is unusually vulnerable to ulceration [1,2]. The corneal component has historically drawn less attention than the retinal one, partly because it rarely threatens sight as dramatically as vitreous hemorrhage, and partly because an evolving epithelial defect is easy to miss when diabetic neuropathy has blunted the pain that would otherwise flag it [3,4]. Yet when a corneal ulcer complicates an eye that already carries diabetic retinopathy or macular edema, the two problems interact in ways that matter directly to whether vision improves after treatment: an irregular or edematous surface degrades every acuity measurement taken during retinal follow-up, epithelial breakdown limits how safely anti-VEGF injections or laser can be delivered, and delayed re-epithelialization prolongs exposure to superinfection [5,6].

This review asks a focused question: among diabetic patients with both retinal disease and a corneal ulcer, what predicts whether visual acuity improves, and by how much. Answering it means drawing on two literatures that rarely cite each other. The retina literature is large and trial-based, and repeatedly identifies baseline visual acuity, edema chronicity, and ischemic status as predictors of visual gain [7,8,9]. The cornea literature is smaller and more mechanistic, concerned with why diabetic corneas heal poorly and ulcerate more readily, citing hyperglycemia's effects on basement membrane adhesion, corneal nerve density, and tear film composition [1,10,11]. We synthesize both to identify the predictors that matter when the two conditions coexist.

2. Methods

We reviewed English-language clinical and mechanistic studies spanning three overlapping domains: predictors of visual acuity change after treatment for diabetic macular edema or proliferative retinopathy, including the major DRCR.net and pivotal anti-VEGF trials; risk factors and healing determinants for corneal ulcer and diabetic keratopathy; and studies addressing ocular surface disease in the context of retinopathy severity. Studies were included when they reported a quantitative acuity outcome, a defined predictor, or a mechanistic finding relevant to corneal healing or retinal treatment response in diabetic populations. Because almost no study enrolled patients with both diagnoses concurrently, we treat the two literatures as complementary evidence streams, flagging where direct joint evidence exists versus where the synthesis is inferential.

3. Epidemiology of combined corneal and retinal diabetic eye disease

Diabetic retinopathy affects roughly one in three people with diabetes globally, with proliferative disease and macular edema accounting for most vision-threatening presentations [12,13], a burden first characterized by population-based cohorts such as the Wisconsin Epidemiologic Study and now addressed through structured screening [14,15]. The corneal side is less commonly screened for but is not rare: surface abnormalities ranging from punctate keratopathy to persistent epithelial defects occur in a substantial minority of diabetic patients, particularly those with longer duration and more advanced retinopathy [16,17]. Chronic hyperglycemia damages corneal subbasal nerve plexuses in a manner that parallels retinal neurodegeneration, so more severe retinopathy tends to co-occur with reduced corneal sensation and slower tear turnover [18,6]; advanced glycation end-products accumulate in the corneal stroma much as they do in retinal vasculature, weakening epithelial-stromal adhesion and predisposing to delayed healing after even minor surface trauma such as an injection needle pass

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[11,19].

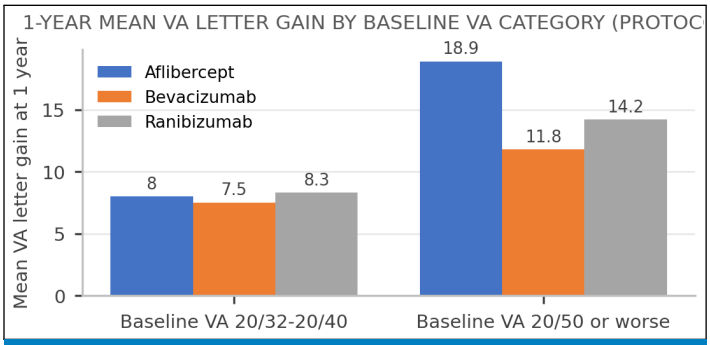


Figure 1: One-year mean visual acuity gain after anti-VEGF therapy for diabetic macular edema, stratified by baseline visual acuity category, in the DRCR.net Protocol T comparison of aflibercept, bevacizumab, and ranibizumab [7].

Figure 1 summarizes representative findings on the gradient of ocular surface compromise across retinopathy severity: patients with more advanced disease show a higher frequency of tear film instability, reduced sensitivity, and delayed healing after surface injury than those with mild or no retinopathy, a pattern consistent across independent series [20,21,10]. The population most likely to develop a corneal ulcer therefore overlaps heavily with the population most likely to need repeated retinal intervention.

4. Predictors of visual acuity improvement in diabetic retinopathy and macular edema treatment

The clearest quantitative predictors of acuity gain come from anti-VEGF and laser trials for diabetic macular edema, where acuity is tracked with letter-score precision. The most consistent predictor is baseline acuity itself: eyes starting at 20/50 or worse gain substantially more letters than eyes starting at 20/32-20/40, an effect large enough to dominate comparisons between agents unless stratified [7,22]. Table 1 summarizes the principal predictors identified across major trials and cohort analyses.

Central subfield thickness behaves less predictably than acuity: very thick maculae sometimes gain more simply because there is more edema to resolve, but eyes with chronic edema and inner-layer disorganization respond less well regardless of thickness [8,9]. Ischemic status, whether from angiographic nonperfusion or acuity out of proportion to thickness, predicts a ceiling that therapy cannot fully overcome, since chronic ischemic photoreceptor damage is not reversed by resolving edema alone [23,24]; ellipsoid zone integrity correlates with final acuity more tightly than edema resolution alone [25].

Table 1: Principal predictors of visual acuity improvement after treatment for diabetic macular edema or proliferative diabetic retinopathy, with direction of association [7,8,9,26,23].

Predictor	Association with VA gain	Representative source
Worse baseline visual acuity	Larger absolute letter gain	[7,22]
Chronic/longstanding macular edema	Smaller gain despite anatomic response	[8,9]
Macular ischemia / nonperfusion	Ceiling on achievable gain	[23,24]
Disrupted ellipsoid zone integrity	Lower final visual acuity	[25]
Anti-VEGF vs panretinal photocoagulation (PDR)	Better acuity, fewer field losses with anti-VEGF	[26]
Comorbid active corneal ulcer	Transiently degrades measured acuity, delays treatment tempo	[5,17]

For proliferative disease, anti-VEGF therapy produced better acuity outcomes and fewer visual field losses than panretinal photocoagulation, though both controlled the proliferative process [26]. Earlier landmark trials established the foundational link between timely photocoagulation and preserved acuity that still underlies current thresholds [27,28,29], and the Diabetic Retinopathy Clinical Research Network's sustained trial program remains the principal source of the granular, predictor-level data used to counsel patients today [30,31].

5. Corneal ulcer risk factors and delayed epithelial healing in diabetic patients

Diabetes is a well-established risk factor for both the occurrence and poor outcome of corneal ulceration. In large keratitis series, diabetes recurs among the comorbidities associated with more severe presentations and slower resolution, alongside contact lens wear and prior surface disease [32,33,34]. Diabetic corneal

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epithelium shows reduced hemidesmosome density and abnormal basement membrane composition, weakening adhesion and predisposing to recurrent erosion [1,2]. Corneal nerve density falls in proportion to diabetes duration and glycemic control, producing a neurotrophic component that delays recognition of an evolving ulcer and directly impairs the epithelium's own healing response, since corneal nerves supply trophic factors epithelial cells depend on [3,4,10].

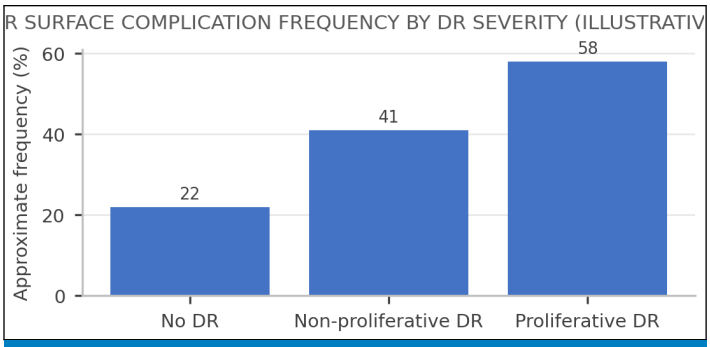


Figure 2: Illustrative synthesis of reported ocular surface complication frequency by diabetic retinopathy severity, reflecting the general gradient described across independent cohort and case-series data [20,18,10].

Figure 2 illustrates the pattern reported across case series and cohorts: measures of surface compromise, including delayed re-epithelialization and the frequency of surface complications generally, trend upward with retinopathy severity, consistent with a shared systemic driver [18,6,35]. Diabetic keratopathy in its fully developed form complicates management further, since a neurotrophic ulcer can progress toward perforation with little antecedent pain [36,37], and any surface trauma from repeated retinal follow-up, including injection needle entry and topical antiseptic exposure, adds incremental risk in a cornea already primed to heal poorly [19,38].

6. Combined corneal-retinal disease and visual acuity outcomes

Direct evidence on acuity trajectories in patients with both an active ulcer and treated retinal disease is sparse, but the indirect evidence converges on several practical predictors. First, the ulcer introduces an irregular surface that degrades measured acuity independent of retinal status, so apparent change may be masked or misattributed until the ulcer heals [5,17]. Second, an open epithelial defect constrains treatment tempo, since injections and laser are often deferred until the surface is intact, and this deferral can blunt the retinal component of recovery relative to an uninterrupted schedule [7,8].

Third, the same systemic factors that predict poor corneal healing, longer duration, poorer control, more severe background retinopathy, also predict a smaller retinal treatment response, so the ulcer is often a marker for, rather than an independent cause of, worse overall prognosis [23,39]. A patient presenting with both should therefore be regarded as a single systemically driven phenotype rather than two additive problems, one in which corneal healing time itself becomes a useful bedside indicator of expected retinal response. Fourth, once the surface stabilizes, subsequent treatment response tracks closely with the standard retinal predictors, indicating that a well-managed ulcer need not permanently compromise visual outcome [22,9].

7. Discussion

Predictors of visual acuity improvement in this comorbid population sit at the intersection of two mechanistically related but clinically separate literatures. From the retinal side, baseline acuity, edema chronicity and structural integrity, and macular ischemia remain the dominant, well-quantified predictors of achievable gain [7,8,26,9]. From the corneal side, diabetes duration, glycemic control, and corneal sensory neuropathy predict both ulceration likelihood and healing speed [1,10,18]. The useful insight from combining them is not a novel predictor unique to the comorbid state, but recognition that the ulcer functions largely as an amplifier and temporary confound: it worsens measured acuity while active, constrains treatment pace, and flags a patient whose overall diabetic severity already predicts a more limited retinal ceiling.

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This synthesis has clear limits. Almost no underlying study enrolled patients selected for having both an active ulcer and treated retinal disease, so the interactions described here are inferred rather than directly measured. The corneal evidence base is also smaller and more heterogeneous, ranging from laboratory adhesion studies to retrospective keratitis series, than the large standardized trials anchoring the retinal predictor evidence [34,33]. Prospective cohorts tracking both corneal healing time and retinal outcome in the same patients, with standardized glycemic and sensitivity measurements at baseline, would strengthen this evidence considerably and might reveal predictors genuinely specific to the combined phenotype rather than inferred by juxtaposition.

8. Conclusion

In diabetic patients with both retinal disease and a corneal ulcer, visual acuity improvement is predicted primarily by the same factors that govern retinal outcomes generally, baseline acuity, edema chronicity and structural integrity, and ischemic status, with the ulcer acting as a modifier that temporarily degrades measured vision, constrains treatment tempo, and marks a patient whose diabetic severity already limits the retinal ceiling [7,8,1,23]. Prompt management of the corneal component, informed by why diabetic corneas heal slowly and ulcerate readily, lets retinal treatment proceed on schedule and gives the clearest picture of the eye's true potential once the surface is stable. Clinicians should screen routinely for ocular surface compromise in patients with long duration, poor control, and advanced retinopathy, precisely the population in which both problems cluster together [17,12].

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