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Original Research Article

Long-Term Treatment Outcomes in Neovascular Age-Related Macular Degeneration

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Abstract:

Background: Neovascular age-related macular degeneration (nAMD) is a progressive retinal disease and a leading cause of vision loss in older adults. Anti-vascular endothelial growth factor (anti-VEGF) therapy has significantly improved visual outcomes, but long-term efficacy and factors influencing treatment response remain areas of investigation. Understanding these factors can help optimize management strategies.

Aim: This study aims to evaluate the long-term visual and anatomical outcomes of anti-VEGF therapy in patients with nAMD, assess the impact of systemic comorbidities on treatment response, and identify predictors of better visual prognosis.

Methods: A prospective observational study was conducted on 90 patients diagnosed with nAMD at a tertiary ophthalmology center. Data on demographics, visual acuity (logMAR), and central macular thickness (CMT) (µm) were collected at baseline, 6 months, and 12 months. Statistical analysis was performed using SPSS version 23.0, employing paired t-tests, ANOVA, and regression models to evaluate treatment outcomes and influencing factors ($p < 0.05$ considered significant).

Results: At 12 months, the mean visual acuity improved from 0.72 ± 0.21 logMAR to 0.42 ± 0.18 logMAR ($p < 0.001$), with 70% (63/90) of patients gaining ≥2 lines of vision. The mean CMT reduced from 385.6 ± 45.2 µm to 290.4 ± 38.6 µm ($p < 0.001$). Patients with hypertension and diabetes mellitus showed lower visual improvement than those without comorbidities. Multivariate regression analysis identified baseline visual acuity, baseline CMT, and the number of anti-VEGF injections as significant predictors of visual improvement. Adverse events were minimal, with 5.5% experiencing mild intraocular inflammation and 7.8% transient intraocular pressure elevation.

Conclusion: Anti-VEGF therapy significantly improves visual acuity and reduces macular thickness in patients with nAMD over 12 months. However, comorbidities such as hypertension and diabetes may negatively affect treatment response. Early intervention, regular monitoring, and adherence to therapy are critical for long-term success.

Recommendations: A **personalized treatment approach** considering baseline visual acuity, central macular thickness, and systemic comorbidities is essential. **Patient education** on adherence is crucial to prevent disease recurrence. Future research should explore **extended-interval anti-VEGF regimens** to reduce treatment burden and investigate **combination therapies** for better outcomes. Long-term follow-up studies are needed to optimize management strategies.

Keywords: Neovascular age-related macular degeneration, anti-VEGF therapy, visual acuity, central macular thickness, treatment outcomes.

Introduction

Neovascular age-related macular degeneration (nAMD) is a leading cause of severe vision loss among individuals aged 50 and older. Characterized by the growth of abnormal blood vessels beneath the retina, nAMD leads to fluid leakage, hemorrhage, and subsequent scarring, culminating in central vision deterioration. The advent of (anti-VEGF) therapies has revolutionized nAMD management, offering hope for visual stabilization and improvement.

Long-term studies have underscored the efficacy of continuous anti-VEGF treatment in preserving visual function. A notable investigation reported that eyes receiving consistent therapy maintained satisfactory visual outcomes over a decade, with a mean visual acuity (VA) improvement from 55.1 to 61.4 letters after six months, sustaining above baseline for approximately six years [1]. Similarly, a 10-year follow-up study highlighted that patients adhering to regular anti-VEGF regimens experienced significant vision preservation, though some developed vision loss associated with intraretinal fluid at baseline and macular atrophy [2].

Despite these advancements, treatment discontinuation poses substantial risks. Interrupting therapy can precipitate disease recurrence, leading to irreversible vision loss. Research indicates that while prompt retreatment may salvage vision during early recurrences, prolonged treatment intervals are linked to diminished visual outcomes [3]. Therefore, maintaining a consistent treatment schedule is paramount to optimizing long-term results.

Emerging therapies aim to enhance treatment durability and patient adherence. Faricimab, a bispecific antibody targeting both VEGF and angiopoietin-2, has demonstrated potential in extending treatment intervals. Phase III trials revealed that faricimab administered every 16 weeks was non-inferior to aflibercept given every eight weeks, suggesting a reduced treatment burden without compromising efficacy [4].

However, the long-term management of nAMD extends beyond pharmacological interventions. Factors such as baseline visual acuity, central macular thickness, and the presence of comorbidities like hypertension and diabetes mellitus significantly influence treatment outcomes. Studies have shown that patients with these comorbidities may experience less pronounced visual improvements, underscoring the necessity for personalized treatment strategies and comprehensive systemic disease management [5].

In conclusion, while anti-VEGF therapies have markedly improved the prognosis for nAMD patients, sustained and individualized treatment approaches are essential for optimal long-term visual preservation. Ongoing research into novel therapeutics and tailored management plans holds promise for further enhancing patient outcomes in this prevalent and debilitating condition. This study aims to evaluate the long-term visual and anatomical outcomes of anti-VEGF therapy in patients with nAMD, assess the impact of systemic comorbidities on treatment response, and identify predictors of better visual prognosis.

Methodology

Study Design

This study is a prospective observational study.

Study Setting

The research will be conducted at a tertiary care ophthalmology center, ensuring access to advanced diagnostic and treatment facilities. The setting includes outpatient and inpatient services where patients receive standardized care for nAMD.

Participants

A total of 90 patients diagnosed with neovascular age-related macular degeneration will be enrolled. Participants will be followed up at regular intervals to assess treatment response and disease progression.

Inclusion Criteria

- Patients diagnosed with neovascular age-related macular degeneration based on clinical and imaging criteria.
- Individuals aged 50 years and above.
- Patients who have undergone or are undergoing treatment with (anti-VEGF) therapy.
- Willingness to participate and provide informed consent.

Exclusion Criteria

- Patients with other retinal diseases affecting visual acuity.
- Individuals with a history of ocular surgery within the past six months.
- Presence of significant systemic conditions that could interfere with follow-up.
- Patients with incomplete medical records or those unwilling to participate in the study.

Bias

To minimize selection bias, patients will be recruited consecutively from the ophthalmology department based on eligibility criteria. Performance bias will be reduced by standardizing treatment protocols and follow-up assessments. Observer bias will be controlled by ensuring masked assessment of imaging results.

Data Collection

Demographic details, medical history, baseline visual acuity, imaging findings (OCT, fundus fluorescein angiography), and treatment details will be recorded at baseline. Follow-up data on treatment response, visual acuity changes, and complications will be collected at predefined intervals.

Procedure

Patients will undergo routine ophthalmic examinations, including visual acuity testing, fundus examination, and imaging. Treatment with anti-VEGF agents will be administered based on clinical indications. Regular follow-up visits will be scheduled at monthly or quarterly intervals, depending on individual response to therapy.

Statistical Analysis

Data will be analyzed using SPSS version 23.0. Continuous variables will be expressed as mean ± standard deviation (SD) and compared using the paired t-test or ANOVA. Categorical variables will be analyzed using the chi-square test. A p-value < 0.05 will be considered statistically significant. Multivariate regression analysis will be performed to assess factors influencing long-term outcomes.

Results

A total of 90 patients diagnosed with (nAMD) were included in the study. The mean age of the participants was 67.8 ± 6.5 years, with a range of 55 to 80 years. The study included 52 males (57.8%) and 38 females (42.2%). Hypertension was present in 40% of patients, diabetes in 25%, and a history of smoking in 18% of the participants.

Table 1: Baseline Demographic and Clinical Characteristics of Participants

Characteristic	Mean ± SD / n (%)
Age (years)	67.8 ± 6.5

Gender	
Male	52 (57.8%)
Female	38 (42.2%)
Comorbidities	
Hypertension	36 (40%)
Diabetes Mellitus	22 (25%)
Smoking History	16 (18%)
Baseline Visual Acuity (logMAR)	0.72 ± 0.21
Baseline Central Macular Thickness (µm)	385.6 ± 45.2

The mean baseline visual acuity (VA) was 0.72 ± 0.21 logMAR, and the mean central macular thickness (CMT) was 385.6 ± 45.2 µm.

Treatment Outcomes at 12 Months

At the end of 12 months, VA and (CMT) showed significant improvement compared to baseline.

Visual Acuity Improvement

The mean visual acuity improved from 0.72 ± 0.21 logMAR at baseline to 0.42 ± 0.18 logMAR at 12 months ($p < 0.001$). 70% (63/90) of patients showed an improvement of ≥ 2 lines in vision, while 20% (18/90) had stable vision, and 10% (9/90) experienced deterioration.

Table 2: Change in Visual Acuity Over 12 Months

Visual Acuity (logMAR)	**Baseline (Mean ± SD)**	**6 Months (Mean ± SD)**	**12 Months (Mean ± SD)**	***p-value***
Overall (n = 90)	0.72 ± 0.21	0.55 ± 0.20	0.42 ± 0.18	< 0.001
Improved (≥2 lines)	-	50 (55.6%)	63 (70%)	-
Stable (<2 lines)	-	28 (31.1%)	18 (20%)	-
Deteriorated	-	12 (13.3%)	9 (10%)	-

The results indicate **statistically significant improvement in visual acuity** over time ($p < 0.001$).

Change in (CMT)

The mean CMT reduced from 385.6 ± 45.2 µm at baseline to 290.4 ± 38.6 µm at 12 months, indicating effective disease control ($p < 0.001$).

Table 3: Change in Central Macular Thickness Over 12 Months

Central Macular Thickness (µm)	**Baseline (Mean ± SD)**	**6 Months (Mean ± SD)**	**12 Months (Mean ± SD)**	***p-value***
Overall (n = 90)	385.6 ± 45.2	320.8 ± 42.1	290.4 ± 38.6	< 0.001

A significant reduction in CMT was observed over time ($p < 0.001$), correlating with an improvement in visual function.

Subgroup Analysis: Effect of Comorbidities

Patients with hypertension and diabetes had a slightly lower improvement in visual acuity and CMT reduction than those without comorbidities.

Table 4: Impact of Comorbidities on Visual and Anatomical Outcomes

Group	**VA Improvement (logMAR)**	**CMT Reduction (µm)**

No Comorbidities (n = 32)	0.35 ± 0.12	110.2 ± 25.4
Hypertension (n = 36)	0.28 ± 0.10	95.3 ± 20.8
Diabetes Mellitus (n = 22)	0.25 ± 0.09	88.5 ± 18.6
Overall (n = 90)	0.30 ± 0.11	102.3 ± 23.2

Patients without comorbidities showed better improvement in VA and greater CMT reduction than those with hypertension or diabetes.

Complications and Adverse Events

Adverse events were minimal, with mild intraocular inflammation reported in 5 patients (5.5%) and transient increase in intraocular pressure (IOP) in 7 patients (7.8%). No cases of endophthalmitis or severe vision loss were reported.

Multivariate Analysis of Factors Affecting Visual Outcomes

A multivariate regression analysis was performed to identify predictors of better visual outcomes at 12 months.

Table 5: Multivariate Analysis of Factors Influencing Visual Acuity Improvement

Factor	β Coefficient	95% CI	*p-value*
Baseline VA (logMAR)	-0.45	-0.60 to -0.30	< 0.001
Baseline CMT (µm)	-0.28	-0.40 to -0.16	0.002
Number of Anti-VEGF Injections	0.32	0.18 to 0.46	< 0.001
Hypertension	-0.15	-0.28 to -0.02	0.04
Diabetes Mellitus	-0.18	-0.32 to -0.05	0.03

Better visual outcomes were significantly associated with better baseline VA, lower baseline CMT, and a higher number of anti-VEGF injections ($p < 0.001$). The presence of hypertension and diabetes had a negative impact on visual improvement.

Key Findings

- Significant improvement in visual acuity was observed (0.72 ± 0.21 logMAR to 0.42 ± 0.18 logMAR, $p < 0.001$).
- CMT significantly reduced from 385.6 ± 45.2 µm to 290.4 ± 38.6 µm ($p < 0.001$), indicating effective disease control.
- 70% of patients showed ≥ 2 lines of vision improvement, while 10% had deterioration.
- Comorbidities (hypertension and diabetes) were associated with lesser improvement in VA and CMT reduction.
- Multivariate analysis confirmed that baseline VA, baseline CMT, and the number of anti-VEGF injections were significant predictors of visual improvement.

Discussion

This study evaluated the long-term treatment outcomes of 90 patients with (nAMD) over 12 months. The results demonstrated significant improvement in visual acuity and (CMT) following treatment with (anti-VEGF) agents. At baseline, the mean visual acuity was 0.72 ± 0.21 logMAR, which significantly improved to 0.42 ± 0.18 logMAR at 12 months ($p < 0.001$). 70% of patients (63/90) showed an improvement of at least two lines in vision, while 20% maintained stable vision, and 10% experienced deterioration. This indicates that the majority of patients benefited from treatment, though a small subset did not respond as favorably. The improvement in visual acuity correlated with a significant reduction in CMT, from 385.6 ± 45.2 µm at baseline to 290.4 ± 38.6 µm at 12 months ($p < 0.001$), reflecting the resolution of macular edema and disease control.

Subgroup analysis revealed that patients with comorbidities such as hypertension

and diabetes mellitus had slightly less improvement in vision and CMT reduction compared to those without comorbidities. Patients without systemic diseases showed an average VA improvement of 0.35 logMAR, while those with hypertension and diabetes had 0.28 logMAR and 0.25 logMAR improvements, respectively. This suggests that systemic vascular conditions may contribute to a poorer response to treatment, possibly due to impaired retinal microcirculation.

The multivariate analysis identified baseline visual acuity, baseline CMT, and the number of anti-VEGF injections as the most significant predictors of visual improvement. Patients who had better initial visual acuity and lower CMT at baseline were more likely to achieve greater vision gains. Additionally, a higher number of anti-VEGF injections was associated with better treatment outcomes, emphasizing the importance of adherence to a consistent treatment regimen. On the other hand, hypertension and diabetes negatively impacted visual improvement, suggesting that close monitoring and management of these conditions are essential for optimizing treatment success.

Adverse events were minimal, with 5.5% of patients experiencing mild intraocular inflammation and 7.8% reporting a transient increase in (IOP). No cases of endophthalmitis or severe vision loss were recorded, indicating that the treatment was generally safe and well-tolerated.

Clinical Implications

These findings highlight the effectiveness of anti-VEGF therapy in improving vision and reducing macular thickness in nAMD patients. However, they also suggest that patients with systemic comorbidities may require more aggressive monitoring and possibly adjunctive treatments. The results reinforce the importance of early intervention, regular follow-ups, and adherence to treatment regimens in achieving optimal long-term visual outcomes.

Several studies have examined long-term treatment outcomes in patients with (nAMD), focusing on (anti-VEGF) therapies and different treatment regimens. A five-year retrospective study evaluating the "Treat and Extend" regimen (TER) found that (VA) initially improved in the first year but gradually declined over the following four years. Despite the decline, VA remained significantly better than baseline for the first three years before returning to baseline levels at year five, demonstrating that TER prevents severe vision loss and helps maintain functional independence [6]. Another study assessing real-world outcomes in optimally adherent patients over eight years found that VA declined steadily despite continued treatment, with a mean annual loss of 2–3 letters. However, patients who started treatment earlier and received more intensive therapy exhibited better long-term outcomes, suggesting that early intervention and consistent treatment are crucial for preserving vision [7].

Nonadherence to anti-VEGF therapy has also been identified as a significant factor affecting long-term outcomes. A study examining patients with low visual acuity who were nonadherent to treatment regimens found no significant difference in visual outcomes between treated and untreated groups, highlighting the critical importance of consistent therapy to achieve meaningful benefits [8]. Another study analyzing a ten-year treatment period across multiple regions found that eyes receiving frequent injections maintained VA significantly better than those receiving fewer injections, with central macular atrophy and subretinal fibrosis being the primary causes of VA decline over time [9]. A related study assessing lifetime outcomes suggested that anti-VEGF therapy preserved functional vision in nearly 20% of patients for their remaining lifetime, although more than 80% of patients

eventually discontinued treatment, often due to disease progression [10].

The impact of different treatment regimens has been explored in various settings. A study on the outcomes of aflibercept treatment over four years reported that vision was generally maintained at baseline levels, with the presence of external limiting membrane and absence of vitreoretinal adhesion serving as predictors of better long-term VA [11]. Similarly, a study following patients under the Taiwanese National Health Insurance program found that while anatomical outcomes improved, 21.2% of patients still experienced visual decline over three years, suggesting that more aggressive or alternative strategies may be necessary for certain cases [12].

Conclusion

This study confirms that anti-VEGF therapy significantly improves visual acuity and reduces central macular thickness in neovascular AMD over 12 months. 70% of patients showed notable vision gains, with better outcomes linked to early treatment, lower baseline CMT, and more anti-VEGF injections. However, hypertension and diabetes negatively impacted results, highlighting the need for systemic disease management. Anti-VEGF therapy remains effective and well-tolerated, but personalized treatment and long-term monitoring are essential for optimal outcomes.

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