


Visual Acuity and Intraretinal Fluid as Predictive Factors for Legal Blindness and Macular Atrophy in Neovascular AMD Eyes Treated with Anti-VEGF: A Swedish Real-World Study

Isac Wickman¹, Ivana Huzevkova¹, Marion Schroeder¹, Elisabet Granstam², Ulrika Kjellström¹, Monica Lövestam-Adrian¹ 

¹Department of Clinical Sciences Lund, Ophthalmology, Lund University, Lund, Sweden; ²Department of Surgical Sciences, Ophthalmology, Uppsala University, Uppsala, Sweden

Correspondence: Isac Wickman, Department of Clinical Sciences Lund, Ophthalmology, Lund University, Lund, Sweden, Tel +46723871926, Fax +4646172721, Email 95isacwickman@gmail.com

Purpose: Ocular coherence tomography (OCT) biomarkers have previously been able to predict low visual acuity (VA). The purpose of this study was to identify other OCT predictors for a final VA ≤ 35 and risk factors for macular atrophy (MA) in eyes with neovascular age-related macular degeneration (nAMD).

Methods: This retrospective observational study included 107 treatment naïve nAMD eyes who initiated treatment and were followed for 3 years \pm 2 months or until VA deterioration to or below 35 ETDRS letters. Eyes with final VA ≤ 35 letters (low VA group) were compared with those with a final VA > 35 letters (maintenance group). Swedish Macula Register (SMR) data and OCT images were analyzed to identify risk factors for MA development and low VA. MA was defined according to the criteria for Complete Retinal Pigment Epithelium and Outer Retinal Atrophy (cRORA), which was based on OCT parameters.

Results: Twenty eyes (19%) were presented with a final VA ≤ 35 ETDRS letters. Mean time from baseline to ≤ 35 ETDRS letters was 587.7 ± 330.4 days, with a mean 9.7 ± 5.3 injections during that period. Mean baseline VA in the maintenance group vs the low VA group were 65.4 ± 10.8 and 52.0 ± 10.6 , respectively; $p < 0.001$. Lower baseline VA was a predictor for low final VA. At baseline, 87% did not have MA on OCT. Among eyes with at least 1 OCT follow-up value in this group, 25% developed MA during the 3-year period. The presence of intraretinal fluid (IRF) at baseline was a predictor for MA development within 3 years in this subgroup.

Conclusion: After 3 years, 19% had declined to VA ≤ 35 ETDRS letters. About 25% with ≥ 1 available OCT follow-ups developed MA. Lower baseline VA predicted a final VA ≤ 35 ETDRS letters in nAMD eyes. IRF at baseline predicted MA. The high prevalence of missing VA values emphasizes the importance of increasing the frequency of VA testing.

Keywords: Swedish macula register, anti-VEGF, macular atrophy

Introduction

Age-related macular degeneration (AMD) is a chronic and progressive disease primarily of the central retina and the most common cause of blindness among the elderly population in the Western World.^{1,2} A continuously aging population will result in increasing cases of AMD worldwide from around 196 million in 2020 to 288 million people in 2040.³ The disease may progress from dry AMD (dAMD) to an exudative form, neovascular AMD (nAMD), which can cause serious visual impairment.⁴ Both dAMD and nAMD eyes have a tendency to progress to macular atrophy (MA) with destruction of photoreceptors, choriocapillaris (CC) and retinal pigment epithelium (RPE).⁵⁻⁷ AMD has been shown to negatively affect variables such as quality of life and driving, and if there is progression to central MA, it can result in loss of the central visual field. Moreover, MA can have a negative effect on visual performance including reading.⁸⁻¹⁰

Today, intravitreal injections with anti-vascular endothelial growth factor (anti-VEGF) are the standard of care for nAMD. The introduction of intravitreal anti-VEGF is believed to have contributed greatly to a reduction of the incidence rate of legal blindness by 50% in nAMD patients above 50 years of age.¹¹ A visual acuity (VA) of 35 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or less is considered the limit for legal blindness.¹²

This level of visual impairment has been shown to have a significantly negative effect on mental health.¹³ Furthermore, eyes at or under the limit for legal blindness have also been found to have a larger proportion of MA and macular hemorrhage at baseline.¹⁴ Such factors underline why a final VA of ≤ 35 ETDRS letters is an important measure of a poor clinical result.

In a 2019 study analysing Swedish Macula Registry (SMR) data, Schroeder et al found that 13% of nAMD eyes presented with vision loss to 35 ETDRS letters or lower 2 years after treatment start.¹⁵ Moreover, Puzo et al also found that 13% of eyes with a baseline VA >35 ETDRS letters had deteriorated to or below 35 ETDRS letters at the 3-year point.¹⁶ Some currently known factors associated with worse VA outcomes despite receiving anti-VEGF treatment are: a lower baseline VA, older age and larger lesion size. The development of MA in the fovea also seems to be related to worse VA outcomes.^{17–19} In the CATT study, 18% of eyes developed MA. Variables commonly associated with the development of MA in nAMD patients include poor baseline VA, retinal angiomatous proliferation (RAP) and intraretinal fluid (IRF) at baseline.^{6,20}

Central retinal thickness (CRT) is an optical coherence tomography (OCT) biomarker that has been used to guide retreatment of nAMD in clinical practice. Recently, however, the presence of fluid in different retinal compartments have emerged as more clinically important OCT-based biomarkers, contributing with better prognostic value for assessment of nAMD.²¹ These biomarkers include subretinal fluid (SRF), which accumulates between photoreceptors and the RPE and has been associated with better visual results as well as reduced occurrence of atrophy. Furthermore, IRF, which is defined as a “cystoid accumulation of fluid within the inner retinal layers”, has been identified as the main negative prognostic biomarker in nAMD, predicting poor visual outcomes.^{22–24} Moreover, the presence of pigment epithelial detachment (PED), ie when the retinal pigment epithelium is detached from Bruch’s membrane, has been associated with negative VA outcomes in nAMD eyes.^{22,25–27}

By 2023, the quality registry SMR covered 87% of all anti-VEGF injections administered to macular degeneration patients in Sweden.²⁸ Registry data is a crucial tool to examine how nAMD patients respond to anti-VEGF treatment in a real-world setting. Supplementing this data with information on the OCT biomarkers referenced above, can be an effective way of understanding how they affect treatment outcomes outside randomized studies. A strength of the retrospective cohort study design is that real-world outcomes can be studied in a natural environment. However, as observed in a prior real-world study, an issue in routine anti-VEGF practice was that there was a significant lack of 1-year follow-up VA values for nAMD patients in Sweden.²⁹ The purpose of the present study was to find predictive factors for visual impairment to 35 ETDRS letters and below, as well as for development of atrophy during 3 years of follow-up, using data from the SMR.

Materials and Methods

Population

This was a retrospective cohort study including 107 treatment naïve eyes with nAMD from 98 patients. All eyes were treated with intravitreal anti-VEGF injections, and treatment was initiated between January 1st 2016 and December 31st 2017 at Skåne University Hospital in Lund. Criteria for inclusion in the study were having a baseline best-corrected visual acuity (BCVA) of >35 ETDRS letters as well as having a follow-up period of at least 3 years \pm 2 months, or permanently deteriorating to VA ≤ 35 ETDRS letters within a 3-year-period. Approval of the study protocol was granted by The Ethics Board of Lund University and the study conformed to the Tenets of the Declaration of Helsinki. The primary outcome of the study was finding predictive factors for visual loss to ≤ 35 ETDRS letters. Secondary outcome measures include the development of MA as well as predictive factors for MA, time from baseline to VA deterioration, number of injections as well as VA development over time.

Originally, 197 eyes receiving injections for a macular neovascularization (MNV) were identified. Ninety eyes were eventually excluded for the reasons presented in Figure 1. The most common cause of exclusion (39 eyes) was loss of follow-up for the following reasons: follow-up was ended due to the clinician's choice (26%), the patient wanted to end follow-ups (23%), deceased patient (28%), patient switching to a clinic whose medical records the authors did not have access to (5%) and unknown (18%).

Variables collected from the registry include sex, age, BCVA, type of MNV lesion, location of the lesion, duration from start of symptoms to attending the clinic and treatment regimen. Variables manually supplemented from patient records were the type and number of injections as well as the number of days of follow-up and days until VA ≤ 35 ETDRS letters. OCT images stored in the IMAGeNet database (Topcon Corporation, Tokyo, Japan) were independently analysed by two physicians (IW and IH). Additional ophthalmology specialists were available for consultation in cases where there was uncertainty or disagreement. The data collectors noted the presence of OCT biomarkers, which consisted of MA, SRF, IRF and PED. The identification of SRF, IRF and PED is illustrated in Figure 2. In cases where a PED was present, its width and height were measured as in Figure 3. BCVA and OCT values were obtained from the first follow-up after a loading dose of 3 injections and from the 1-, 2- and 3-year follow-ups ± 2 months. Due to the retrospective design of the study, there were missing follow-up VA and OCT data as specified in the results section. Eyes were divided into two groups depending on VA outcomes; the "maintenance group" remained above 35 ETDRS letters during the entire follow-up period, while the "low VA group" deteriorated to or below 35 ETDRS letters during the follow-up period. If an eye would recover VA and then remain above 35, it was included in the maintenance group. The eyes that recovered and then deteriorated definitely were included in the low VA group. Definite deterioration was defined as the final timepoint when VA reached ≤ 35 letters without recovering, meaning that either this was the final recorded VA or there were subsequent VA values registered but these did not surpass 35 ETDRS letters. VA values had been entered in the SMR as ETDRS letters or Snellen values. In cases where only Snellen values were entered, they were converted to ETDRS letters in accordance with Gregori et al 2010.³⁰

In the present study, MA was defined according to the criteria for Complete RPE and Outer Retinal Atrophy (cRORA) defined by Sadda et al 2018³¹: (1) region of hypertransmission of at least 250 μm in diameter in any lateral dimension, (2) zone of attenuation or disruption of the RPE of at least 250 μm in diameter, and (3) evidence of overlying photoreceptor degeneration", see Figure 4 RPE tears were excluded from the definition.³¹ In terms of PED dimensions, greatest height

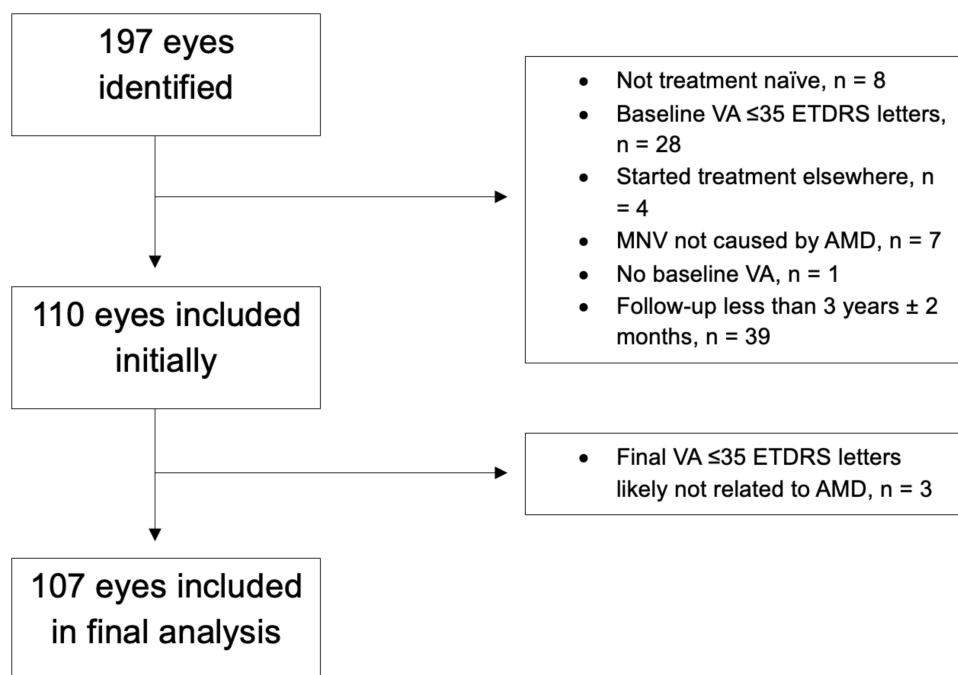


Figure 1 Flow-chart showing reasons for exclusion from the study.

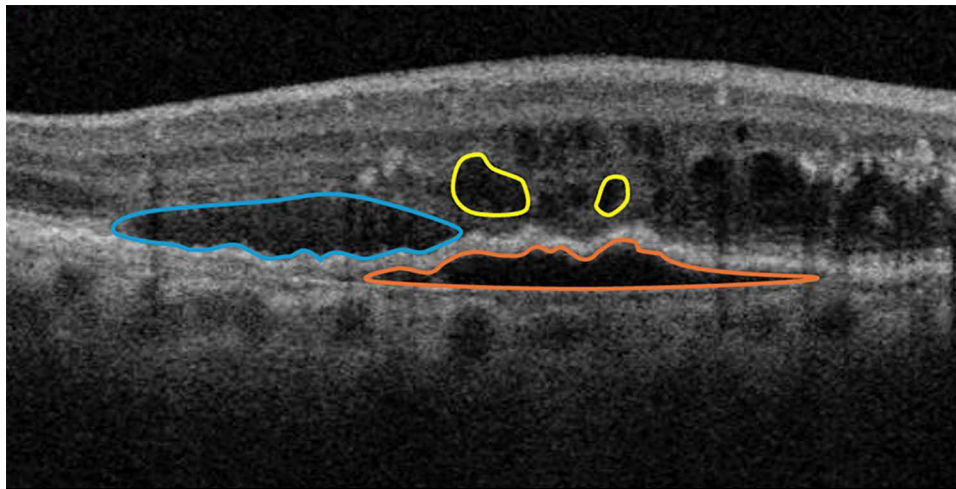


Figure 2 An optical coherence tomography (OCT) B-scan showing macular neovascularization (MNV) with subretinal fluid (SRF) in blue, pigment epithelial detachment (PED) in Orange and intraretinal fluid (IRF) of which some have been highlighted in yellow.

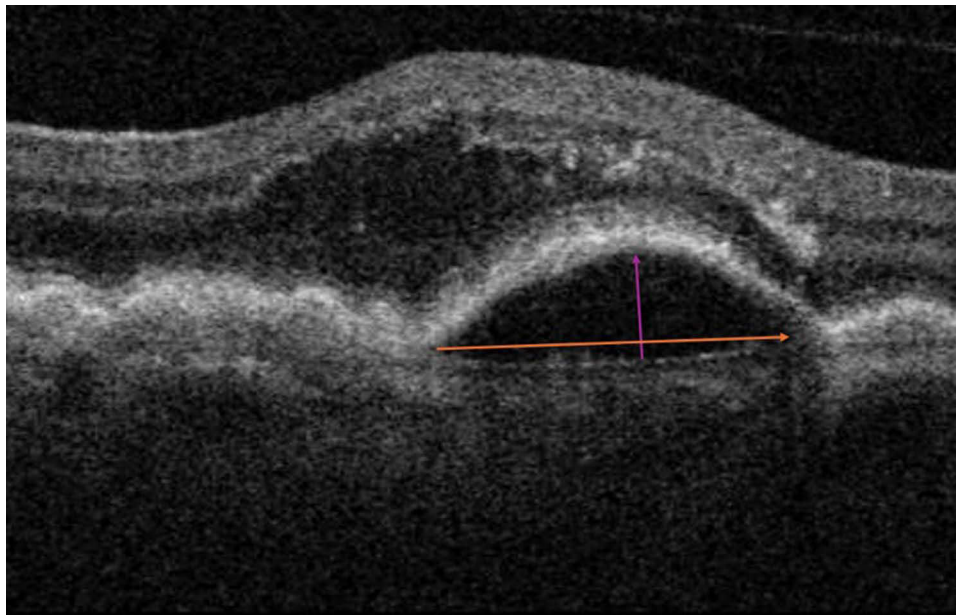


Figure 3 An optical coherence tomography (OCT) B-scan showing how pigment epithelial detachment (PED) width [Orange arrow] and height [purple arrow] were measured.

was measured from Bruch’s membrane to the RPE as the highest vertical distance, and greatest width was measured as the greatest horizontal diameter at the lesion site. IRF was defined as intraretinal “hyporeflective cystoid spaces” on OCT, and SRF was defined as a “nonreflective space between the posterior boundary of the neurosensory retina and the retinal pigment epithelium (RPE)/choriocapillaris signal”.^{21,32} OCT biomarkers were only registered in the study if they were present inside the inner macular ring of the standard ETDRS grid as seen in [Figure 5](#).

Statistical Analysis

Data analysis was performed using SPSS 29 (IBM). Descriptive statistics were analyzed using means and standard deviation for continuous variables while frequencies and percentages were used for categorical variables. Regarding baseline characteristics as well as change in VA, Mann–Whitney *U*-test was used for comparison of continuous variables. Chi-squared test, Fisher’s exact test or Fisher-Freeman-Halton exact test was used for categorical data. A Kaplan–Meier

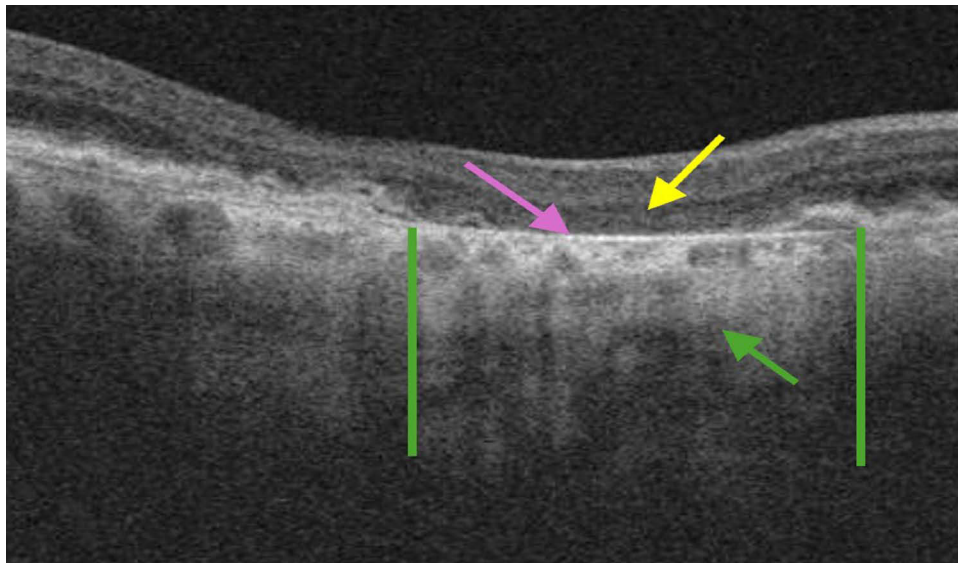


Figure 4 An optical coherence tomography (OCT) B-scan showing complete RPE and outer retinal atrophy (cRORA), with photoreceptor degeneration [yellow arrow], RPE disruption [purple arrow] and an area of hypertransmission [green arrow and lines].

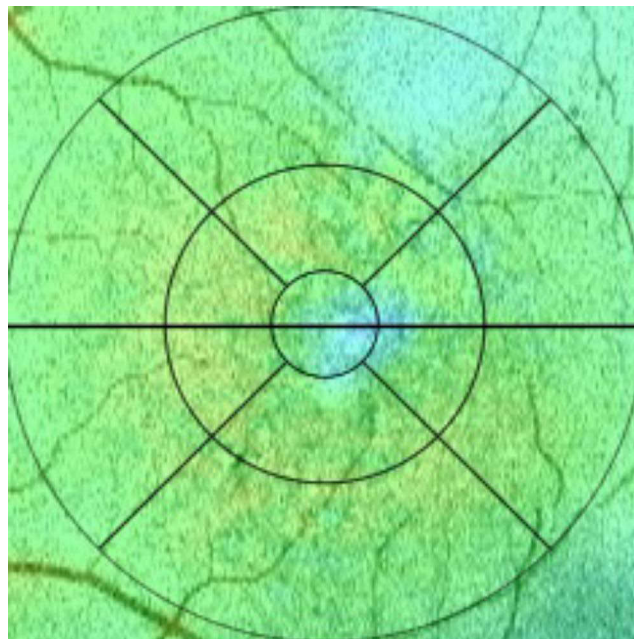


Figure 5 Image showing Early Treatment Diabetic Retinopathy Study (ETDRS) grid including the inner macular ring, which consists of the two innermost circles.

curve was plotted to show survival time for eyes in the low VA group. Multivariate logistic regression analysis was performed to find predictive factors for vision loss to ≤ 35 ETDRS letters as well as to identify predictors for MA.

Results

Baseline Characteristics

As seen in [Table 1](#), the 20 eyes (19%) that permanently declined to VA ≤ 35 letters were named the low VA group, and the 87 eyes (81%) that maintained their VA were called the maintenance group. VA was significantly higher at baseline for the maintenance group, while PED width was significantly larger in the low VA group. There were no significant

Table 1 Baseline Characteristics, Drug Choice and Treatment Regimen in Maintenance Group vs Low VA Group.

Baseline Characteristic	Both Groups	Maintenance	Low VA	P-value
No. of eyes, n (% of patients)	107 (100)	87 (81)	20 (19)	
Sex, n (% of patients)				
Female	70 (71)	55 (70)	15 (79)	0.419
Mean age (SD)	77.7 (8.2)	77.2 (8.0)	80.1 (9.1)	0.261
Mean ETDRS letters (SD)	62.9 (12.0)	65.4 (10.8)	52.0 (10.6)	<0.001
Membrane type, n (% of eyes)				0.437
Type 1	42 (39)	37 (43)	5 (25)	
Type 2	30 (28)	23 (26)	7 (35)	
Type 3	21 (20)	15 (17)	6 (30)	
PCV	4 (4)	4 (5)	0	
Undetermined	10 (9)	8 (9)	2 (10)	
Lesion location, n (% of eyes)				0.311
Subfoveal	40 (37)	30 (35)	10 (50)	
Juxtafoveal	27 (25)	25 (29)	2 (10)	
Extrafoveal	15 (14)	12 (14)	3 (15)	
Undetermined	25 (23)	20 (23)	5 (25)	
Symptom duration, n (% of eyes)				0.460
0–<2 months	62 (58)	51 (59)	11 (55)	
2–<4 months	17 (16)	14 (16)	3 (15)	
4–6 months	17 (16)	15 (17)	2 (10)	
>6 months	11 (10)	7 (8)	4 (20)	
Initial drug, n (% of eyes)				1.000
Aflibercept	102 (95)	83 (95)	19 (95)	
Ranibizumab	5 (5)	4 (5)	1 (5)	
Initial treatment regimen, n (% of eyes)				0.322
T&E	93 (87)	75 (86)	18 (90)	
PRN	2 (2)	1 (1)	1 (5)	
Fixed	12 (11)	11 (13)	1 (5)	
PED present on OCT, n (%)	102 (95)	83 (95)	19 (95)	1.000
Mean PED height (SD), n = 102	247.5 (209.2)	235.5 (209.7)	300.3 (203.9)	0.128
Mean PED width (SD), n = 102	1994.0 (1225.2)	1828.5 (1110.1)	2717.2 (1460.0)	0.014
Atrophy on OCT, n (% of eyes)	14 (13)	11 (13)	3 (15)	0.723
Subretinal fluid on OCT, n (% of eyes)	92 (86)	74 (85)	18 (90)	0.732
Intraretinal fluid on OCT, n (% of eyes)	80 (75)	63 (72)	17 (85)	0.243

Abbreviations: ETDRS, Early Treatment Diabetic Retinopathy Study; PCV, polypoidal choroidal vasculopathy; T&E, Treat & Extend; PRN, Pro Re Nata; PED, pigment epithelial detachment; OCT, optical coherence tomography.

differences regarding demographic data, symptom duration, injection type, treatment regimen, fluid distribution on OCT, PED height, presence of MA on OCT, membrane type or lesion location.

Visual Acuity

As seen in [Table 1](#), mean baseline VA for all participants was 62.9 ± 12 letters. In the maintenance group, mean baseline VA was 65.4 ± 10.8 letters vs 52 ± 10.6 letters in the low VA group, respectively. There were missing VA values at the 1-, 2- and 3-year follow-ups. These, together with the mean baseline VA for each group, are described in [Table 2](#). At the 1-year follow-up, mean VA change was 3.5 ± 11.8 letters vs -12.8 ± 21 letters in the maintenance group and in the low VA group, respectively; $p = 0.009$. After 2 years, the mean change of VA was $+2.8 \pm 11.5$ letters in the maintenance group vs -19.9 ± 16.5 letters in the low VA group; $p < 0.001$. Mean baseline VA was 66.1 ± 10.9 and 49.4 ± 9.2 , respectively. At the 3-year follow-up, mean VA change was $+1.7 \pm 12.4$ letters in the maintenance group vs -27.3 ± 16.9

Table 2 The Number of Eyes in the Maintenance Group vs the Low VA Group with an Available VA Value After 1, 2 and 3 Years.

Year	1	2	3
Maintenance group eyes, n (% of eyes)	69 (79)	62 (71)	57 (66)
Maintenance group mean baseline VA (SD)	65.9 (10.7)	66.1 (10.9)	65.6 (10.6)
Low VA group eyes, n (% of eyes)	9 (45)	9 (45)	3 (15)
Low VA group mean baseline VA (SD)	52.7 (13.5)	49.4 (9.2)	44.3 (7.0)

Notes: The mean baseline VA for each group is also included.

letters in the low VA group; $p = 0.009$. For the 20 eyes in the low VA group, the mean duration until VA ≤ 35 ETDRS letters was 587.7 ± 330.4 days, see [Figure 6](#).

Number of Injections

In the low VA group, the mean number of injections administered until VA ≤ 35 ETDRS letters was 9.7 ± 5.3 . The mean number of injections administered per year in the maintenance group is presented in [Table 3](#). Not all eyes were in treatment constantly during the three-year-period; some stopped treatment and were just followed-up clinically, while others stopped treatment to restart it during the 3-year period.

Predictive Factors for ≤ 35 ETDRS Letters

A univariate logistic regression analysis followed by stepwise multiple logistic regression analysis to adjust for potential confounders, found baseline VA to be a predictor of ≤ 35 ETDRS letters before and after adjusting for age, sex and the presence of IRF at baseline (adjusted odds ratio [AOR], 0.902; 95% C.I. 0.854–0.952; $p < 0.001$). No other baseline variable was a statistically significant predictor of low VA.

MA Development and Predictive Factors for MA

At baseline, 93 eyes (87%) had no MA present on OCT. The focus will now be on this subgroup. After receiving an initial loading dose of anti-VEGF, 5 eyes (6%) had MA present. At the 1-year follow-up, 13 eyes (15%) had MA on OCT. After 2 years, 18 (23%) of eyes had MA present. At the 3-year follow-up, 18 eyes (25%) had MA present. All eyes

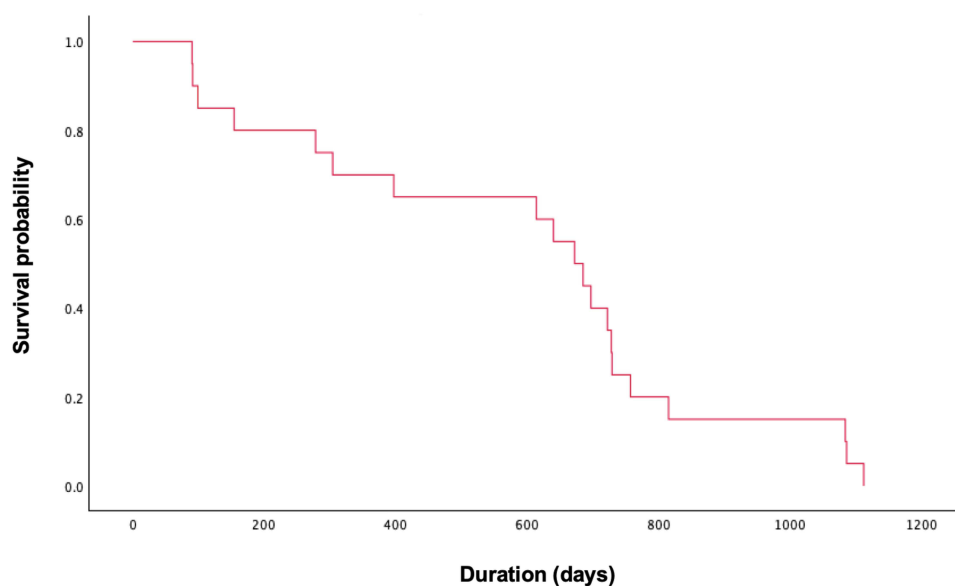


Figure 6 Kaplan–Meier curve showing the number of days from baseline to VA ≤ 35 in the low VA group.

Table 3 The Number of Injections for Eyes in the Maintenance Group, from Baseline to Year 3

Year	1	2	3	Total
Mean	8.4	6.5	6.2	20.4
Standard deviation	1.9	2.7	2.9	6.5
Eyes, n	87	86	80	87

Table 4 Out of the 93 Eyes Without MA on OCT at Baseline, This Table Shows the Number of Eyes with Available OCT Images at Different Checkpoints

Time Point	After Loading Dose	After 1 Year	After 2 Years	After 3 Years
Eyes, n (% of eyes)	91 (98)	87 (94)	78 (84)	71 (76)

in the subgroup except for one, had at least one OCT value beyond baseline. During the 3-year-period overall, 23 eyes (25% of eyes with a follow-up value) developed MA. Among the group without atrophy at baseline, 68 eyes (73%) had presence of central IRF at baseline. In the group where MA developed at some point, 22 eyes (96%) had IRF at baseline vs 46 eyes (66%) in the group where MA was not seen; $p = 0.005$. The proportion of eyes missing OCT follow-ups are presented in [Table 4](#).

A univariate logistic regression analysis followed by stepwise multiple logistic regression analysis found IRF at baseline to be a predictor of MA development before and after adjusting for age, VA and SRF (AOR, 10.820; 95% C.I. 1.344–87.110; $p < 0.025$). No other baseline variables were identified as statistically significant predictors of MA.

Discussion

The present study analyzed a cohort of 107 eyes with nAMD that were followed for three years. Two subgroups with a final VA of ≤ 35 letters vs a final VA of > 35 letters were compared. Twenty out of 107 eyes (19%) reached ≤ 35 letters, which is the functional limit for legal blindness. This number is slightly higher than the 13% that Schroeder et al 2019 found for a follow-up period of 2 years in a Swedish nation-wide registry study, as well as the 13% that were found by Puzo et al 2024 to drop to ≤ 35 letters after 3 years in a Spanish multicenter registry study. Furthermore, the mean time from baseline to ≤ 35 letters in our study was 588 days, which equates to 19 months. This is substantially longer than the 10 months shown by Schroeder et al 2019.^{15,16} One likely explanation for the differences between our study and the latter in terms of both duration until VA deterioration and the number of eyes with low VA, is that the present study had a 3-year follow-up period as opposed to 2 years. Another potential contributor to the differences between the present study and the two mentioned above, could be that our study included eyes starting treatment in a single center as opposed to including national multi-center data, since there might be differences between patient groups and treatment outcomes between different clinics.

In the present study, the low VA group presented with a significantly larger PED width than the maintenance group at baseline. However, we did not identify PED width as a predictor for MA or low VA. Previously, it has been suggested that PED width predicts progression to nAMD, however a study by Cheong et al 2020 showed that neither PED width nor height predicted VA outcomes in eyes with nAMD.^{33,34} Apart from the maintenance group having a significantly higher VA at baseline than the low VA group, and the former having a significantly smaller PED width, the two groups were homogenous in terms of baseline variables. This indicates the importance of the degree of visual impairment at baseline for the result of treatment. The mean VA gain after 3 years in the maintenance group was 1.7 letters. This is lower compared with real-world evidence from Eleftheriadou et al 2018 and Rayess et al 2015, who showed a 66 letter and a 13.6 letter gain after 3 years, respectively.^{35,36} In the maintenance group in our study, the mean number of injections were 8.4 ± 1.9 , 6.5 ± 2.7 and 6.2 ± 2.9 for year 1, 2 and 3, respectively. In the study by Eleftheriadou et al, the median number of injections in year were 8, 4 and 4 for the respective years, while the mean number of injections in the

study by Rayess et al was 76 ± 18 , 5.7 ± 2.3 and 5.8 ± 2.1 . These numbers are somewhat similar, hence the difference in 3-year VA results may not be explained by differences in injection quantity. Furthermore, the comparison does not include the low VA group in our study, which will likely have shifted the mean VA change towards the positive side. However, in the present study, the mean baseline VA of patients who had a 3-year VA value in the maintenance group was 65.6 ± 10.6 letters. This is more than 10 letters higher than in the study by Eleftheriadou et al 2018. Moreover, mean baseline VA in the study by Rayess et al was significantly lower at 20/120 Snellen equivalent (approximately 46 ETDRS letters) for the eyes that had a 3-year VA follow-up. Hence, the higher mean baseline VA in the present study could be one explanation for the relatively modest VA change after 3 years.

A logistic regression analysis showed that a lower baseline VA was a predictor of a final VA of ≤ 35 letters for nAMD eyes treated with anti-VEGF. This is consistent with previous evidence showing that a lower baseline VA predicts a lower final VA in this patient group,^{12,15,37} hence further supporting the role of baseline VA as an important prognostic factor for treatment outcomes in nAMD patients. However, in their study, Puzo et al 2024 showed that 43% of patients with a baseline VA of < 35 letters, had a VA of > 35 letters after 3 years, with 8% of them obtaining a VA of ≥ 70 letters.¹⁶ This indicates that there might be potential value in continued treatment in such patients. However, their study is not completely comparable to ours, since we only included eyes with a VA of > 35 letters at baseline. Nevertheless, it is an idea for future studies to include patients with lower VA as well.

In the subgroup analysis of patients without MA at baseline, 25% of eyes who had at least one follow-up OCT image after baseline presented with MA involving the macula on OCT at some point during the 3-year period. While existing numbers of MA incidence vary as well as follow-up lengths, our study is relatively consistent with previous studies. One example is a study by Spooner et al, which showed that 27% of eyes on a treat and extend (T&E) regimen vs 25% on a pro re nata (PRN) regimen developed MA after 4 years of follow-up. It is noteworthy, however, that their definition of MA differed slightly, and they used both OCT and fundus autofluorescence (FAF) images.³⁸ Eng et al 2020 had a 564% incidence of new cases of cRORA in a 2-year period, and in the CATT study, 18.3% of patients developed MA after 2 years.^{6,39} In the present study, the presence of IRF on baseline OCT was shown to be a predictor variable for MA development. This is consistent with previous evidence showing that it is a risk factor for MA.^{6,40}

Previously known predictors for MA development did not prove statistically significant in our study, one of them being membrane type. This might be partly explained by the study's relatively small sample size and the fact that the membrane type in 9% of eyes in the study were registered as "undetermined" in SMR. Visual acuity was another variable that did not predict MA. A partial explanation for that could be that we, as mentioned above, excluded eyes with a VA of 35 letters or less. This is in contrast to in the CATT study, where eyes with a lower baseline VA were included in the analysis of risk factors for MA.⁶ Another possible explanation for the fact that other variables did not prove significant in predicting MA, is that atrophic lesions had to fulfil the criteria for cRORA outlined by Sadda et al 2018 in order to count as MA. This differs from some studies and is, in a way, a more binary way of categorizing MA as it does not take into consideration atrophy types such as incomplete Retinal Pigment Epithelial and Outer retinal atrophy (iRORA). For example, previously, it has been indicated that there is an association between the presence of SRF and a better visual prognosis, which could not be shown in this study.³² Recently, deep learning based solutions for the identification and measuring of OCT biomarkers have emerged, and they could help to make the process more efficient for both researchers and clinicians in the future and contribute to further insights about the role of such biomarkers in nAMD progression and severity.^{41,42}

A limitation of the study is its retrospective study design, which is one reason for the number of missing OCT and VA data at follow-ups. Previous studies have shown that eyes lost to follow-up tend to have worse final observed VA, indicating that estimates of overall VA results could be falsely skewed in a positive direction.^{43,44} The lack of VA follow-up values in this study was not necessarily only related to loss to follow-up, but it is nonetheless an important point to keep in mind when drawing conclusions from such results. For clinics to better monitor nAMD patients' VA, more VA follow-ups are needed as it is an important factor in monitoring treatment response. A strength of the study, however, is that it uses real-world data showing nAMD eyes in a true clinical setting.

Conclusions

In conclusion, the present study confirmed that a lower baseline VA predicts a final VA of 35 ETDRS letters or less. Furthermore, IRF was a predictor for the development of MA. This confirms the findings of previous studies and further emphasizes the need for automated ways of identifying and quantifying predictive biomarkers such as IRF to help accurately guide treatment. Moreover, the number of missing follow-up VA values in this real-world study indicates the need for more clinic appointments including VA testing.

Abbreviations

AMD: Age-related macular degeneration; dAMD: Dry age-related macular degeneration; nAMD: Neovascular age-related macular degeneration; MA: Macular atrophy; CC: Choriocapillaris; RPE: Retinal pigment epithelium; Anti-VEGF: Anti-vascular endothelial growth factor; VA: Visual acuity; ETDRS: Early treatment diabetic retinopathy study; SMR: Swedish Macula Register; RAP: Retinal angiomatous proliferation; IRF: Intraretinal fluid; CRT: Central retinal thickness; OCT: Optical coherence tomography; SRF: Subretinal fluid; PED: Pigment epithelial detachment; MNV: Macular neovascularization; cRORA: Complete RPE and Outer Retinal Atrophy; T&E: Treat and extend; PRN: Pro re nata.

Data Sharing Statement

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the Regional Ethical Review Committee, Lund, Sweden (approval number 2017/807). Access to registry data was granted by SMR:s steering committee. Informed consent was obtained from all participants.

Consent for Publication

Written consent has been obtained from the patient for the images used in [Figures 2 to 5](#). It is available upon request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

MLA is a consultant for Novartis, Bayer AG, Allergan, Roche. She has received funding from Bayer AG and Novartis. EG is/has been a member of advisory boards for Abbvie, Novartis, Bayer AG, Roche. She has held lectures for and received fees from Novartis, Bayer AG, Allergan, Novo Nordisk. MS is a consultant for and has received funding from Bayer AG. IW, IH and UK report no competing interests in this work.

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