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Treatment outcomes of Age-Related Macular Degeneration Among a Group of Patients in Albania

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Abstract

Background: Age-related macular degeneration (AMD) is the leading cause of vision loss in people over 50 years old. The appropriate treatment is essential for vision preservation. Information about AMD treatment in our country is insufficient. In this context, the aim of this study was to evaluate the effects of anti-VEGF therapy in a group of AMD patients in Albania.

Methods: A pre-test post-test study was carried out among AMD patients being referred to the Ophthalmology Service at the University Hospital Center "Mother Teresa", in Tirana, Albania, during 1 December 2020 – 30 November 2021. After excluding confounding conditions, a total of 120 patients were appropriate to participate. Visual acuity and macular central thickness was measured in both right and left eye of participants and compared across different moments of treatment regime.

Results: The mean age of the patients was 73.4 years ± 2.33 years (50% female, 28.3% rural residency). The mean value of visual acuity was 21.4% and 20.3% in the right and left eye, respectively, before treatment, whereas the respective mean values of central thickness were 317mm and 330mm. After each anti-VEFG injection, there was a significant increase of mean visual acuity in both right and left eye, and a significant reduction of mean central thickness as well. Visual acuity and central thickness were inversely associated.

Conclusion: Anti-VGEF treatment of AMD is effective as it is associated with a significant

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improvement of the visual acuity and macular central thickness in AMD patients.

Keywords: Albania, age-related macular degeneration, anti-VGEF, central thickness, visual acuity.

INTRODUCTION

Age-related macular degeneration (AMD) is an eye disease that affects central vision. AMD is a common condition: it is a leading cause of vision loss in people over 50 years old. AMD does not cause complete blindness, but loss of central vision can make it harder to see faces, read, drive, or work up close, such as cooking (1,2).

There are two forms of AMD: dry and wet. Dry AMD is a fairly common condition. About 80% (8 out of 10) of people who have AMD have the dry form. There is still no way to treat dry AMD (2).

Wet AMD is less common, but much more serious. Visual loss occurs faster with wet AMD than with dry AMD. Many people do not realize they have AMD until their vision is very blurred. Therefore, it is important to make regular visits to an ophthalmologist.

Some of the symptoms include blurred (low) vision, empty or dark spots in the field of view, distortion of images or the appearance of waves or curves in straight lines, etc. Age-related macular degeneration risk factors include: AMD family history, smoking, increased exposure to oxidative stress, saturated fat diet, high blood cholesterol, overweight, hypertension, age over 60 years, heart disease, etc. (3).

Diagnosis of AMD involves physical examination of the eye, Amsler grid test, Optical Coherence Tomography (OCT) and Coherent Optical Tomography Angiography (OCTA).

Treatment of AMD depends on the disease form. Dry AMD is not curable (4). Wet AMD can be treated with anti–vascular endothelial growth factor (anti-VEGF) therapy. The treatment protocol and the duration of the injections are based on some important parameters, including vision measurement, with and without correction, and measurement of central thickness in the macula, central thickness. Also, based on these parameters, it is determined the effect of the applied injections is determined (5).

In Albania there is no data on the effects of treatment of age-related macular degeneration. In this context, this study aimed to evaluate the effects of anti-VEGF therapy in a group of AMD patients in Albania.

METHODS

This is a pre-test post-test study carried out among AMD patients being referred to the Ophthalmology Service at the University Hospital Center “Mother Teresa”, in Tirana, Albania, during the period 1 December 2020 – 30 November 2021.

Study population

During this period, among the patients being referred to our Service with a suspected diagnosis of "age-related macular degeneration", 120 of them resulted in decreased vision and thus suitable to be included in the actual study. These patients were carefully examined in order to identify other conditions that affect vision loss or deterioration. These include moderate or advanced cataract, as well as other potential conditions that may affect vision independently

of AMD. In case of evidence of these conditions, these patients were excluded from the study, in order to avoid the confounding of the results by other known factors that may also affect the vision in AMD patients. Any patient with pseudophakia or cataract at an early stage was deemed fit to be included in the current study. These conditions were met by a total of 120 patients with AMD, and therefore these patients constituted the final study population. Among these, 60% had pseudophakia while the remaining 40% had early-stage cataract.

Data collection

General information was retrieved from the patients at the time of their presentation at the Ophthalmology Service. Data regarding the presence of other concomitant conditions were obtained from relevant examinations and tests.

The diagnosis of AMD was established through vision measurement, fundus oculi examination on bio microscope where various macular atrophies were observed, CNV (choroidal layer neo vases) and by measuring macular central thickness. Visual acuity of each eye for every patient was performed through the Snellen test. The measurement of the central thickness of the macula in each eye was performed through the Optical coherence tomography (OCT). OCT looks for details in the retina, macula, and optic nerve that cannot be seen during lens examination. This apparatus scans the retina and provides very detailed images of the retina. During this examination, the thickness of the center of the macula or what is called Central thickness is measured, which is one of the criteria for the therapy to be followed.

Treatment of AMD in the patients included in the study consisted of monthly intravitreal injections of anti-VEGF agents.

Data related to the results of examinations for the vision acuity and the central thickness of the macula for each eye and for each patient were recorded at the initial moment (at the time of diagnosis before treatment) and then at each moment of the application of each subsequent session of therapy.

Statistical analysis

Absolute numbers and corresponding percentages were used to describe categorical variables; for describing continuous or discrete numerical variables, the arithmetic mean (magnitude of central tendency) and standard deviation (magnitude of dispersion) was used.

The chi square test was used to compare categorical variables. To compare the mean value of the dependent variable according to the categories of the independent variable, the non-parametric Friedman test k related samples was used for.

The Spearman's rho correlation coefficient was used to assess the strength of the relationship between the numerical variables in the study; this test accounts for the violations of the normal distribution requirements of the numerical variables under consideration.

In all cases the observed statistical associations were considered statistically significant if the P-value <005.

Data analysis was performed through the Statistical Package for Social Sciences software, version 20.

RESULTS

The study involved 120 patients with the final diagnosis Age-Related Macular Degeneration (AMD). The mean age of the patients in the study was 73.4 years ± 2.33 years, ranging from 48 years (1 patient) to 90 years (1 patient). About one third of the patients (32.5%) were 70 years old or younger at the time of the study, 19.2% were in the age group 71-75 years, 31.7% were in the age group 76-80 years and the rest of 16.7% were over 80 years old. Half of the patients in the study were male. Meanwhile 71.7% of the patients in the study lived in the urban areas while the remaining 28.3% lived in rural areas. The prevalence of smoking among study participants was 41.7%, 55% had hypertension and 2.5% had a family history for AMD (Table 1).

Table 1. General information about study participants

Variable	Number	Percentage
Total	*120*	*100.0*
Age (in years)	73.4 ± 2.33 *	
Age-group		
≤70 years old	39	32.5
71-75 years old	23	19.2
76-80 years old	38	31.7
>80 years old	20	16.7
Sex		
Male	60	50.0
Female	60	50.0
Residence		
Urban	86	71.7
Rural	34	28.3
Smoking		
No	70	58.3
Yes	50	41.7
Hypertension		
No	54	45.0
Yes	66	55.0
Family history for AMD *		
No	116	97.5
Yes	3	2.5

* Mean value ± standard deviation.

** Any discrepancy with the total number is due to missing information.

Table 2 shows the mean values of vision acuity in different moment of treatment. It can be noticed that before the injection (during the first visit) the mean value of the vision in the right eye of the patients was 21.44% while in the left eye it was 20.34%. It is also observed that, after each injection, the mean value of the visual acuity increases almost monotonously for both the right and the left eye. For example, the mean value of vision acuity in the right eye goes from 21.44% before treatment (first visit) to 23.86% in the second injection, 26.80% in the third injection, 29.17% in the fourth injection, increasing more further to 29.66% in the fifth injection, 32.58% in the sixth injection and 37.4% in the ninth injection. The increase in the mean value of patients' vision acuity during the treatment time (or after each treatment session) is statistically significant (P <0.001) for both the right and the left eye (Table 2).

Table 3 shows the level of visual acuity impairment at different moments of treatment. It can be noted that after each injection, the proportion of patients with severe damage in the right and left eye is reduced significantly (P<0.05) and varying from 36.4% before treatment (first visit) to 31% in the second injection, 25.2% in the third injection, 24.6% in the fourth injection, 23.2% in the fifth injection, 18.6% in the sixth injection and decreasing further to 11.8% in the ninth injection (P<0.001 for the linear trend of reduction).

Table 4 shows the mean value of the central thickness before treatment and at different moments during treatment. It can be noticed that there is a clear decreasing linear trend of this parameter with the course of treatment sessions: with the increase of the number of treatment sessions the average value of the central thickness

Table 2. Mean visual acuity (in%) in the right and left eye of AMD patients, before treatment and during treatment

Statistical parameter	**Before treatment**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 9**	**P-value**
RIGHT eye								
Mean value	21.44%	23.86%	26.80%	29.17%	29.66%	32.58%	37.94%	**<0.001***
Standard deviation	21.90%	21.34%	22.48%	24.14%	25.48%	26.28%	24.88%	
LEFT eye								
Mean value	20.34%	23.92%	26.93%	28.78%	29.15%	30.26%	33.33%	**<0.001***
Standard deviation	21.70%	21.90%	21.97%	23.58%	24.17%	25.43%	28.26%	

* P-value according to Frideman non-parametric test for k related samples.

Table 3. Level of visual acuity impairment in the right and left eye of AMD patients, before treatment and during treatment

Variable	Before injection	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 9	P-value
RIGHT eye								
Level of visual acuity impairment								
Severe (<10%)	43 (36.4)*	36 (31.0)	26 (25.2)	16 (24.6)	13 (23.2)	8 (18.6)	2 (11.8)	**0.021****
Average (10-50%)	66 (55.9)	70 (60.3)	64 (62.1)	38 (58.5)	31 (55.4)	24 (55.8)	10 (58.8)	
Mild (>50%)	9 (7.6)	10 (8.6)	13 (12.6)	11 (16.9)	12 (21.4)	11 (25.6)	5 (29.4)	
LEFT eye								
Level of visual acuity impairment Severe								
(<10%)	44 (37.9)	36 (31.6)	24 (23.8)	14 (21.2)	11 (18.6)	8 (17.0)	3 (15.8)	**0.015****
Average (10-50%)	66 (56.9)	68 (59.6)	63 (62.4)	41 (62.1)	38 (64.4)	30 (63.8)	11 (57.9)	
Mild (>50%)	6 (5.2)	10 (8.8)	14 (13.9)	11 (16.7)	10 (16.9)	9 (19.1)	5 (26.3)	

* Absolute number and column percentage (in parenthesis).

** P-value according to chi square test.

NOTE: Any discrepancy with the total number is due to missing information.

Table 4. Mean values of Central thickness (in mm) in the right and left eye of AMD patients, before treatment and during treatment

Statistical parameter	Before treatment	Visit 3	Visit 4	Visit 6	Visit 9	P-value
RIGHT eye						
Mean value	316.38	266.83	211.47	187.72	172.00	**<0.001 ***
Standard deviation	100.13	69.899	55.897	54.842	59.028	
LEFT eye						
Mean value	330.16	286.79	249.80	216.76	191.77	**<0.001 ***
Standard deviation	115.41	85.626	82.439	47.804	28.810	

* P-value according to Frideman non-parametric test for k related samples.

decreases significantly (P<0.001) both in the right and in the left eye (negative relationship).

Table 5 shows the level of central thickness at different moments of treatment. It can be noted that after each injection, the proportion of patients with edematous macula in the right and left eye is reduced significantly (P<0.05) and varying, for example, from 81.4% before treatment (first visit) to 60.4% in the third injection, 32.7% in the fourth injection, 25% in the sixth injection and decreasing further to 16.7% in the 9th injection in the right eye (P<0.001 for linear trend of reduction).

Table 6 shows the bivariate correlation coefficients (Spearman's rho coefficient) between central thickness (in mm) and visual acuity (in %) for the right eye and for the left eye of AMD patients, in different moments during treatment. Before and at any time during treatment, there is a negative relationship between these two parameters meaning that as central thickness decreases the visual acuity improves and vice-versa. For the right eye, there is a moderate, negative, and statistically significant relationship between visual acuity and central thickness at the time of the initial visit and at the third injection; during subsequent injections the relationships are not significant. A similar situation is observed in the left eye, with significant relationships before treatment, and during 3rd and 4th injection, and then the relationship loses significance (probably due to the very small number of patients available for analysis at these late stages).

Table 5. Level of Central thickness in the right and left eye of AMD patients, before treatment and during treatment

Variable	Before treatment	Visit 3	Visit 4	Visit 6	Visit 9	P-value
RIGHT eye						
Level of central thickness						
Dry (<180)	5 (4.2)*	4 (4.0)	13 (26.5)	15 (41.7)	6 (50.0)	**<0.001****
Normal (180-240)	17 (14.4)	36 (35.6)	20 (40.8)	12 (33.3)	4 (33.3)	
Edematous (>240)	96 (81.4)	61 (60.4)	16 (32.7)	9 (25.0)	2 (16.7)	
LEFT eye						
Level of central thickness						
Dry (<180)	5 (4.3)	4 (4.0)	6 (12.2)	6 (15.8)	4 (30.8)	**<0.001**
Normal (180-240)	14 (12.1)	24 (23.8)	21 (42.9)	19 (50.0)	8 (61.5)	
Edematous (>240)	97 (83.6)	73 (72.3)	22 (44.9)	13 (34.2)	1 (7.7)	

* Absolute number and column percentage (in parenthesis).

** P-value according to chi square test.

NOTE: Any discrepancy with the total number is due to missing information.

Table 6. Bivariate correlations between central thickness and visual acutiy in the right and left eye of AMD patients, before treatment and during treatment

Central thickness (in mm)	**Visual acuity (in %) – RIGHT eye**				
	Before treatment	**Visit 3**	**Visit 4**	**Visit 6**	**Visit 9**
Before treatment	**-0.378***				
Visit 3		**-0.222***			
Visit 4			-0.234		
Visit 6				-0.190	
Visit 9					-0.381
Central thickness (in mm)	**Visual acuity (in %) – LEFT eye**				
	Before treatment	**Visit 3**	**Visit 4**	**Visit 6**	**Visit 9**
Before treatment	**-0.396***				
Visit 3		**-0.302***			
Visit 4			**-0.380***		
Visit 6				-0.219	
Visit 9					-0.368

* Correlation is statistically significant (P<0.05).

DISCUSSION

Age-related macular degeneration (AMD) is a condition that affects a relatively large number of individuals worldwide. A systematic literature review and meta-analysis published in 2014 reported that AMD is responsible for about 9% of all blindness cases worldwide, constituting the most common cause of blindness in developed countries and AMD prevalence is expected to increase as a result of the exponential growth of the elderly population (6). Prevalence of AMD in all regions of the world is strongly and positively related to age, according to the international literature (7,8).

Early stage AMD is more prevalent in Europe, Oceania and North America and less prevalent in Asia, while later stage AMD is more prevalent in Oceania, Europe and less prevalent in Latin America and the Caribbean (6).

In terms of the total number of people affected by AMD, in 2020 there were about 196 million people affected by any form of AMD worldwide and this number is expected to increase to around 290 million in 2040, where the largest number of cases is expected to be in Asia (113 million), while Europe it will be in second place with about 69 million people affected by AMD, followed by Africa with 39 million people affected, Latin America and the Caribbean with 39 million cases, North America with 25 million cases and finally Oceania with 2 million expected cases (6). Of course, these numbers depend on the size of the population in these regions of the world.

Another literature review and meta-analysis published in 2020 reported that Europe is facing

a demographic transition due to the aging population leading to an increase in demand for health-related diseases related to age-related diseases, which of course includes age-related macular degeneration (9). AMD is the leading cause of blindness in the world, as we noted earlier in our discussion, and it is also the leading cause of blindness in Europe (9). Although antivascular therapy with endothelial growth factor (anti-VEGF) has revolutionized the treatment of neovascular AMD, again this health condition requires significant resources for health care for these patients (9).

There are generally no gender differences related to AMD prevalence; (6,7,9) this is also supported by the data of our study, where 50% of AMD patients were female and 50% were male.

In terms of the effects of AMD treatment on visual acuity and macular central thickness, different studies report different results. A study of 2,072 patients (2,577 eyes) examining the effect of injections (33,187 injections) with endothelial growth factor (VEGF) in patients with AMD, those with diabetic macular edema (DME), and patients with retinal venous occlusion (RVO) and myopic choroidal neovascularization (CNV) over 5 years, reported that visual acuity improved in patients with AMD during the first year of treatment; then a decrease in visual acuity of >15 letters was observed in about 5.3% of AMD patients, in 56% of them the vision acuity remained stable and in 10% the visual acuity increased by >15 letters (10). These data are in line with the findings of our study as in our patients we also noticed an improvement of visual acuity during the treatment injection sessions that lasted about 9 months. However, the above study reported that the improvement in visual acuity observed in patients with AMD during the first year could not be maintained longer despite the increase in the number of injections.

Data from the international literature suggest that anti-VEGF therapy is associated with improved visual acuity or vision in patients with AMD (11,12), a finding that is fully consistent with the results of our study.

Another study reported improved visual acuity after anti-VEGF injections and the increase in the number of injections was associated with greater improvement in visual acuity; with the proper frequency of injections a stabilization or improvement of visual acuity was achieved for almost 90% of patients. This finding is also consistent with the result of our study where by the 9th injection about 80-90% of patients had an improvement in visual acuity compared to the situation before the treatment injections. The international literature suggests that the appropriate number of injections is about 7 injections per year (13).

A meta-analysis comparing the effectiveness and safety of different types of anti-VGEF therapy (intravitreal bevacizumab, ranibizumab and aflibercept) for patients with choroidal neovascular macular degeneration (cn-AMD), diabetic macular edema (DME), edema of retinal vein occlusion (RVO-MO) and choroidal myopic

neovascularization (m-CNV), concluded that the choice of anti-VEGF agent may depend on the specific condition of the retina, basal visual acuity, and treatment regimen (14).

A study examining the association between visual acuity and macular central thickness in patients with AMD, DME, and RVO concluded that there was a moderate negative correlation between these two parameters (correlation coefficient -0.24) at the initial patient examination and thereafter, a result that is quite similar to the result in our study where the correlation coefficient between visual acuity and the central thickness of the macula was -.378 in the right eye and -0.396 in the left eye. The association of visual acuity with the central thickness of the macula was also reported by other studies (15,16).

CONCLUSION

Anti-VGEF treatment of AMD is effective as it is associated with a significant improvement of the visual acuity of AMD patients, and it improves the thickness of the macula as well. Based on these results, it is necessary to promote and apply the treatment of AMD through anti-VEGF preparations as these are quite effective in treating this health condition. Of course, treatment should be individualized according to the characteristics and condition of patients, and in accordance with the international guidelines.

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REFERENCES

1. American Optometric Association. Macular degeneration. https://www.aoa.org/healthy-eyes/eye-and-vision-conditions/macular-degeneration?sso=y.

2. Coleman HR, Chan CC, Ferris FL III, Chew EY. Age-related macular degeneration. 2008.

3. Gupta OP, Brown GC, Brown MM. Age-related macular degeneration: the costs to society and the patient. Curr Opin Ophthalmol 2007;18(3):201-5.

4. Brown MM, Brown GC, Stein JD, Roth Z, Campanella J, Beauchamp GR. Age-related macular degeneration: economic burden and value-based medicine analysis. Can J Ophthalmol 2005;40(3):277-87.

5. Clemons TE, Milton RC, Klein R, Seddon JM, Ferris FL 3rd; Age-Related Eye Disease Study Research Group. Risk factors for the incidence of Advanced Age-Related Macular Degeneration in the Age-Related Eye Disease Study (AREDS) AREDS report no. 19. Ophthalmology 2005;112(4):533-9.

6. Wong WL, Su X, Li X, Cheung CM, Klein R, Cheng CY, Wong TY. Global prevalence of age-

related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health 2014;2(2):e106-16.

7. Rudnicka AR, Jarrar Z, Wormald R, Cook DG, Fletcher A, Owen CG. Age and gender variations in age-related macular degeneration prevalence in populations of European ancestry: a meta-analysis. Ophthalmology 2012;119(3):571-80.

8. Kawasaki R, Yasuda M, Song SJ, Chen SJ, Jonas JB, Wang JJ, Mitchell P, Wong TY. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. Ophthalmology 2010;117(5):921-7.

9. Li JQ, Welchowski T, Schmid M, Mauschitz MM, Holz FG, Finger RP. Prevalence and incidence of age-related macular degeneration in Europe: a systematic review and meta-analysis. Br J Ophthalmol 2020;104(8):1077-1084.

10. Wecker T, Ehlken C, Bühler A, Lange C, Agostini H, Böhringer D, Stahl A. Five-year visual acuity outcomes and injection patterns in patients with pro-re-nata treatments for AMD, DME, RVO and myopic CNV. Br J Ophthalmol 2017;101(3):353-359.

11. Brown DM, Kaiser PK, Michels M, Soubrane G, Heier JS, Kim RY, Sy JP, Schneider S; ANCHOR Study Group. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med 2006;355(14):1432-44.

12. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, Kim RY; MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355(14):1419-31.

13. Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group, Martin DF, Maguire MG, Fine SL, Ying GS, Jaffe GJ, Grunwald JE, Toth C, Redford M, Ferris FL 3rd. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology 2012;119(7):1388-98.

14. Pham B, Thomas SM, Lillie E, Lee T, Hamid J, Richter T, Janoudi G, Agarwal A, Sharpe JP, Scott A, Warren R, Brahmbhatt R, Macdonald E, Straus SE, Tricco AC. Anti-vascular endothelial growth factor treatment for retinal conditions: a systematic review and meta-analysis. BMJ Open 2019;9(5):e022031.

15. Bell KJ, Hayen A, Glasziou P, Mitchell AS, Farris M, Wright J, Duerr HP, Mitchell P, Irwig L. Early CRT monitoring using time-domain optical coherence tomography does not add to visual acuity for predicting visual loss in patients with central retinal vein occlusion treated with intravitreal ranibizumab: A Secondary Analysis of Trial Data. Retina 2017;37(3):509-514.

16. CATT Research Group, Martin DF, Maguire MG, Ying GS, Grunwald JE, Fine SL, Jaffe GJ. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. N Engl J Med 2011;364(20):1897-908.