ORIGINAL PAPER

Correlation Between the Findings of Optical Coherent Retinal Tomography (OCT), Stereo Biomicroscopic Images from Fundus of an Eye and Values from Visual Acuity of Diabetic Macular Edema

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ABSTRACT

Introduction: Diabetic maculopathy is the major cause of reduced visual acuity in patients with non-proliferative diabetic retinopathy and occurs on average in 29% of patients who have diabetes for 20 or more years. **Aim:** The aim of this study is to re examine the correlation between the findings of optical coherence retinal tomography, stereo bio-microscopic images from fundus of an eye and values from visual acuity of diabetic macular edema. In addition, the aim is to show the importance of various ophthalmic tests for establishing diagnosis in time. **Material and methods:** The research sample consisted of 90 subjects-patients from Cabinet for photographic documentation, fluorescein angiography and laser photocoagulation in Department of Ophthalmology at the University Clinical Centre in Sarajevo. The study was a one-year long, prospective, clinical study. **Results:** Research has shown a positive correlation between the various tests that are applied for the diagnosis of diabetic macular edema. Accurate and early diagnosis is of great importance for the treatment in time of this disease by applying laser photocoagulation, intravitreal injections of Anti-VEGF drugs or surgical treatment by Pars Plana Vitrectomy.
Key words: diabetic macular edema, visual acuity, optical coherence tomography, fundus stereo biomicroscopy

1. INTRODUCTION

Diabetic maculopathy is the major cause of reduced visual acuity in patients with non-proliferative diabetic retinopathy and occurs on average in 29% of patients who have diabetes for 20 or more years (1). Previous research discovered that the prevalence of diabetic maculopathy is proportional to duration of diabetes (2). The most important change that occurs in diabetic maculopathy is diabetic macular edema. Maculopathy usually defines the presence of retinal edema in the area of the posterior part of the eye that structurally and functionally damages the macular region (3). Macular edema is defined as the accumulation of liquids and other substances (lipids, proteins), which leads to a thickening of retinal tissue and its functional decrease. The cause of macular edema emergence, pathophysiology explains by the disturbed functioning of hemato-retinal barrier (4). Inflammatory factors and increased levels of vascular endothelial growth factors a involved in establishing macular edema (5). In addition to medical history, diagnosis can be established on the basis of ophthalmic findings: of visual acuity, stereo bio-microscopic fundus examination, recording and analyzing computerized retinal tomography (OCT) (6. 7), fundus imaging (FF), fluorescein angiography (FA) (8, 9, 10).

2. AIM OF RESEARCH

The aim of this study is to re examine the correlation between the findings of optical coherence retinal tomography, stereo bio-microscopic images from fundus of an eye and values from visual acuity of diabetic macular edema. In addition, the aim is to show the importance of various ophthalmic tests for establishing diagnosis in time.

3. MATERIALS AND METHODS

Approach to the study was based on set objectives by choosing the most homogenic sample to minimize the poly-causality of observed parameters. The patients have all fulfilled the inclusion criteria:

Patients older than 50 years, both sexes, where the diagnosis of diabetes is discovered at least 12 months prior to inclusion in the study.

Patients who are not suffering from other chronic diseases such as hypertension, end stage renal disease, anaemia, infectious diseases and other systemic diseases.

Following subjects are excluded from the research:

- Patients who have other eye diseases: monoculus, eye injuries, earlier eye surgery, glaucoma, uveitis, cataracts, degenerative disease, retinal and chorioidal detachment .
- Patients who underwent panretinal laser photocoagulation as well as patients who received intravitreal therapy.
- In patients with diabetic maculopathy who have "high risk" proliferative retinopathy, which can lead to severe vision loss, panretinal laser photocoagulation is urgently indicated.

The study sample consisted of 90 subjects-patients from Cabinet for photographic documentation, fluorescein angiography and laser photocoagulation in Department of Ophthalmology at the University Clinical Centre in Sarajevo. All patients were diagnosed with clinically significant diabetic on macular edema in at least one eye. 90 selected participants were formed into three groups based the value of the best corrected central visual distance acuity. The study was a one-year long, prospective study. All patients completed the following ophthalmological tests: determination of best corrected visual acuity at distance of 6m using a Snellen's optotype, Goldmann's Applanation tonometry, bio-microscopic examination of anterior and posterior eye segment and computerized tomography of the retina.

Based on best corrected central visual distance acuity, three groups were formed:

- Group I: 30 patients whose best corrected visual acuity was 0.7 or better.
- Group II: 30 patients whose best corrected visual acuity was before 0.2 to 0.6.
- Group III: 30 patients whose best corrected visual acuity was 0.1 or less.

Determination of visual acuity (VA): Best corrected visual acuity(BCVA) was measured at 6m distance without correction or with the appropriate corrections using the Snellen optotype. For examining the anterior and posterior eye segment was used bio-microscope with Slit light (SLIT LAMP: LSL 532S MOD. 1449-675. Carl Zeiss Meditec AG.JENA, Germany). Establishment of CSME diagnosis based on stereo bio-microscopic fundus examination was done based on the ETDRS criteria for defining the CSME. Only for the purpose of this research was formed gradation scale, so that this finding could be included in the statistical analysis. All diagnosed diabetic maculopathies were classified into four gradation scale groups and marked with levels .

Coherent tomography of the retina (OCT) was performed on all patients at beginning of the research on the device (STRATUS OCT. MODEL 3000th Carl Zeiss Meditec, JENA GERMANY).
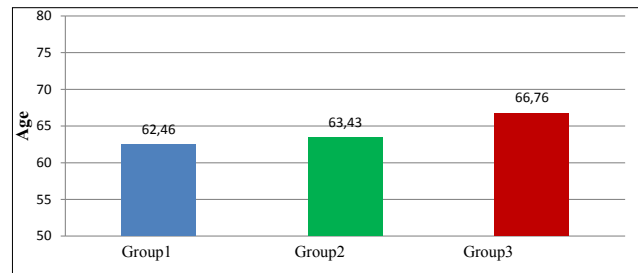
Statistical data analysis: nominal and ordinal variables in the study were analyzed by $\chi2$ test, and on the lack of expected frequencies Fisher's exact test was used. For continuous variables in the study, the symmetry of their distribution was firstly analyzed using the Kolmogorov-Smirnov test. When the distribution of continuous variables was symmetrical, the arithmetic mean and the standard deviation were used to show the average value and measures of dispersion.

For comparison of variables were used parametric tests (student's-test and ANOVA test, paired t test).

Chart 1. *Age structure of subjects*

	Control Variables		Subject age	Duration of DM	HbA1c	Visual acuity before LFK
Groups	Subject age	Correlation	1.000	0.303	0.129	-0.106
		Significance (2-tailed)	.	0.004	0.227	0.322
		Df	0	87	87	87
	Duration of DM	Correlation	.303	1.000	0.253	-0.261
		Significance (2-tailed)	0.004	.	0.017	0.013
		Df	87	0	87	87
	HbA1c	Correlation	0.129	0.253	1.000	-0.235
		Significance (2-tailed)	0.227	0.017	.	0.027
		Df	87	87	0	87
	Visual acuity before treatment	Correlation	-0.106	-0.261	-0.235	1.000
		Significance (2-tailed)	0.322	0.013	0.027	.
		Df	87	87	87	0

Table 1. *Correlation of independent variables (group) in relation to the dependent variable age of the patients, duration of DM, HbAc1 values and visual acuity before LFK*

Bio- microscopic fundus findings, by leveling scale		Group			Total
		Group 1	Group 2	Group 3	
Level 2	Number	19	10	3	32
	%Percentage	63.3%	33.3%	10.0%	35.6%
Level 3	Number	11	19	17	47
	% Percentage	36.7%	63.3%	56.7%	52.2%
Level 4	Number	0	1	10	11
	% Percentage	0.0%	3.3%	33.3%	12.2%
Total	Number	30	30	30	90
	% Percentage	100.0%	100.0%	100.0%	100.0%

Table 2. *Categorization of bio- microscopic fundus (eye) findings, by leveling scale, before LFK*

Group		Average value	Number	Std. Deviation	Std. Error
Group 1	TMV before LFK	7.7890	30	.78545	.14340
Group 2	TMV before LFK	9.1762	30	1.70183	.31071
Group 3	TMV before LFK	9.8915	30	2.09726	.38290

Table 3. *Average values of TMV before LFK inside subject groups*

Group		N	Average	Std. Deviation	Minimum	Maximum
Group 1	FT before LFK	30	281.66	60.426	204.00	499.00
Group 2	FT before LFK	30	406.86	115.170	235.00	684.00
Group 3	FT before LFK	30	445.20	123.283	240.00	759.00
P<0.05						

Table 4. *The differences in average values FT before LFK, inside subject groups*

OCT qualitative		Group			Total
		Group 1	Group 2	Group 3	
Level 1	Number	16	1	0	17
	% Percentage	94.1%	5.9%	0.0%	100.0%
Level 2	Number	11	7	1	19
	% Percentage	57.9%	36.8%	5.3%	100.0%
Level 3	Number	3	18	13	34
	% Percentage	8.8%	52.9%	38.2%	100.0%
Level 4	Number	0	4	16	20
	% Percentage	0.0%	20.0%	80.0%	100.0%
Total	Number	30	30	30	90
	% Percentage	33.3%	33.3%	33.3%	100.0%

Table 5. *Display of qualitative OCT findings within subject groups according to leveling scale*

When the distribution of continuous variables was unsymmetrical, for showing average value and a measures of dispersion were used median and interquartile range, and for their comparison nonparametric tests (Mann-Whitney U test, Kruskal-Wallis test). For the statistical analysis of obtained date was used the software system SPSS for Windows (version 20.0, SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel (version 2010, Microsoft Corporation, Redmond , WA, USA).

4. DISCUSSION

Diabetic retinopathy, as the complication of diabetes manifests on the eyes, is one of the leading causes of blindness in developed countries (11). In highly developed countries such as the United States, each year is registered 5,000 new cases of legally defined blindness and morbidity costs exceed 620 million dollars (12). This research pays great attention to the diagnosis of diabetic macular edema, which is based on a medical history, a standard eye examination and specific findings for this disease: stereo bio-microscope fundus examination, recording and analyzing computerized tomography of the retina (OCT), fundus images (FF) and fluorescein angiography (FA). Early Treatment Diabetic Retinopathy Study (ETDRS) defines clinically significant macular edema (13, 14). The numerical value, total macular volume (TMV) and central foveolar thickness (FT)

can be clearly monitored and evaluated. The average value of TMV under physiological conditions is 6-7 cubic mm. The study involved subjects with values greater than 7 mm cubic. The average value for FT in the center of the foveola is about 170-190 microns, so that the edema is defined with the value of the FT that is more than 200 microns. Ideal treatment of diabetic maculopathy is prevention, which is proven by studies of Diabetic Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS). However, despite of prevention, diabetic maculopathy can appear as the first sign of diabetes. As soon as clinically significant macular edema (CSME) is diagnosed, treatment should be started (15).

According our results : Age of the patients is correlated with the duration of diabetes mellitus; older respondents have a longer duration of diabetes mellitus df = 87, p = 0.004. With other variables, age is not correlated. Duration of diabetes is correlated with age (p = 0.004), with average values of HbA1c (p = 0.017), and negatively correlated with visual acuity before LFK (p = 0.013). Average values of HbA1c are correlated with the duration of diabetes mellitus and negatively correlated with visual acuity before LFK (p = 0.027). Visual acuity before LFK is negatively correlated with the duration of diabetes mellitus and average values of HbA1c. Visual acuity is decreased when values of HbA1c are increased and when the subject is longer a diabetic.

Most of the subjects from group 1 during bio-microscopic fundus examination before LFK had level 2, 19 (63.3%), and then grade 3, 11 (36.7%). No subjects had level 4 before LFK. Most subjects from the group 2 during bio-microscopic fundus examination, before LFK, had level 3, 19 (63.3%), and level 2, 10 (33.3%). Whereas, only one subject had a level 4 before LFK. Most subjects from the group 3 during bio-microscopic fundus examination, before LFK, had level 3, 17 (56.7%), and level 4, 10 (33.3%). Only 3 (9.4%) patients had level 2 before LFK. Chi square test showed a statistically significant difference in the leveling group during bio-microscopic fundus examination before LFK. The best results on level 1 had the group 1. χ^2=30.82, p<0.005.

The lowest average value of TMV before LFK had subjects from the group 1. Subjects from group 1 had statisticaly significant low value FT before LFK (p<0,05). Chi square test showed a statistically significant difference in leveling by qualitative OCT findings within a group, χ^2=65.706, p=0.001. The largest number of subjects from group 1 has a level 1, and most of the subjects from group 3 has a level 4.

Analyzing the age structure of subjects in the group, we see that diabetic retinopathy with clinically significant maculopathy usually occurs in the age group 50-70 years of age. Here we must bear in mind that this study was limited to subjects older than 50 years of age. Looking at groups, average age of the group 1 was 62.46 years, the average age of

the group 2 was 63.42 years, while the average age of the subjects from group 3 was 66.76 years. Moss and Klein (1994) obtained similar results in their study (16). Alice M, Lesley H, G Bradley, Jonathan W, Arliene R, Paul P and associates (2008) in their study concluded that the average age of patients with diabetic maculopathy was 76 years (17). Since their subjects' average age was higher by about 10 years we must seek an explanation in the fact that their subjects had previously been treated for diabetic maculopathy. Krushkal-Wallis nonparametric test showed that there was no statistically significant difference in the average number of subjects' years within the group, and that the respondents in terms of age were nearly equalized. This study demonstrated no statistically significant difference between the sexes when it comes to diagnosis of diabetic maculopathy. The results show that among the total subjects were 46 male and 44 female patients. Paerson's chi square test showed that there was no statistically significant difference in prevalence between men and women among the studied groups. Also, no significant correlation between gender and the analyzed parameters VO, the fundus findings, OCT's done before LFC. These results correspond to the results of other researchers. Similar results were published in 1991, a research group ETDRS Report Number 9 (18). Alice M, Lesley H, G Bradley, Jonathan W, Arliene R, Paul P and associates (2008) in their study concluded that from the total number of subjects 40% were females (17). The study found that the average duration of diabetes mellitus in group 1 was 10.63 years, average duration of diabetes mellitus in group 2 was 14.46 years and the average duration of diabetes mellitus in group 3 was 18.66 years (Table 4). Krushkal-Wallis nonparametric test showed a statistically significant difference in the average duration of diabetes mellitus between the groups, and that the questioned groups compared to the duration of diabetes mellitus in patients differ substantially. Subjects from third groups have diabetes mellitus the longest, while the ones from first group, the shortest. The explanation of this statistical difference between the groups in duration of diabetes till the point of starting treatment, we need to search on the cultural, socio-economic and war grounds. Davis and associates (1992) have explored both types of diabetes, and concluded that diabetic retinopathy (DR), as a complication after 10 years of diabetes, occurs in approximately 50% of patients, 75% after 20 years of age and 90% of patients after 30 years of age (19). Kohner (1999) in his study states that patients with type II diabetes, i.e. 5% of them, have distinct elements of the DR during establishing diagnosis of diabetes, and approximately 20% of patients have symptoms of DR after two years of diagnosis. Statistics after 10 or more years is the same like the one for patients of type I (20). Different from the research of Kohner and associates, this research was limited by the inclusion criteria on subjects of particular age, whose diabetes was previously diag-

nosed while newly detected diabetes was not in the study. Tushar and Stuart (2009) in their research discovered that the prevalence of diabetic maculopathy is proportional to duration of diabetes (2). In that study, all patients were analyzed for HbA1c- an indicator of sugar levels in blood during three months. Earlier in the discussion it was stated that the regulation of sugar in blood, blood pressure and lipid regulation was the first step in the treatment of diabetic maculopathy. This is why (inclusion criteria) in the study did not participate subjects with elevated blood pressure. HbA1c, on average, was increased in all groups. ANNOVA test showed that there was no statistically significant difference in average values of HbAc1 between the groups (Table 1).

The arisen conclusion is that increased HbA1c call for better glycemic control in patients with diabetic maculopathy. Kollias and Ulbig (2010) in their study reported that the incidence of diabetic retinopathy is decreasing by 76% in patients whose HbA1c is 7.2% compared to 47% of patients whose HbA1c is 9.1% (21). Tushar R, Stuart F. (2009) in their research discovered that the prevalence of diabetic maculopathy is proportional to lesser control of diabetes (20). Yang X, Liu K, Xun X. (2009) in their studies came to similar conclusions (22). Schmid, Neumaier, Stolba and Binder in their research (2006) discovered that there was no statistically significant difference between HbA1c and the effect of laser photocoagulation in DME (23). Sim and his associates established a statistically significant correlation between OCT and values of visual acuity in patients with diabetes mellitus (24).

5. CONCLUSION

Research has shown a positive correlation between the various tests that are applied for the diagnosis of diabetic macular edema. Accurate and early diagnosis is of great importance for the treatment in time of this disease by applying laser photocoagulation, intravitreal injections of Anti-VEGF drugs or surgical treatment by Pars Plana Vitrectomy. For the accurate and in time diagnosis of CSMO it is necessary to apply multiple methods and tests within the ophthalmological examination. The importance is reflected by the fact that the applied therapeutic methods lead to operational invasive methods that irreversibly alter retina. As soon as clinically significant macular edema (CSME) is diagnosed, treatment should be started. Therapy in due course improves the quality of patients' life and delays serious complications of diabetic retinopathy in the eye. Each applied diagnostic method has its own importance in monitoring any anatomical or functional changes in the eye. By using multiple methods, the disease and the changes it's causing are understandable. In addition, information provided by the diagnostic methods not only directing therapy but also have a great significance for the prognosis and treatment. Applied diagnostic methods i.e. severity of findings, accompanied by numerical values, are positively correlated.

CONFLICT OF INTEREST: NONE DECLARED

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