Saidin Nor-Masniwati^{1,2}, Bethel Indira Livingstone^{3,4}, Ab Rahman Azriani⁵, Embong Zunaina^{1,6 *}

¹Department of Ophthalmology and Visual Science, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

²Department of Ophthalmology, Hospital Tuanku Ampuan Najihah, 72000 Kuala Pilah, Negeri Sembilan, Malaysia

³Department of Ophthalmology, Hospital Tuanku Ja'afar, 70300 Seremban, Negeri Sembilan, Malaysia

⁴Mawar Medical Centre, 70300 Seremban, Negeri Sembilan, Malaysia

⁵Department of Community Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

⁶Hospital Universiti Sains Malaysia, Jalan Raja Perempuan Zainab II, Kubang Kerian, Kelantan, Malaysia

*Corresponding author: Embong Zunaina E-mail: <u>zunaina@usm.mv</u>

Received 25 May 2022 Revised 28 Sept 2022 Accepted 30 Nov 2022 Published Online 23 Dec 2022

Evaluation of Visual Acuity, Contrast Sensitivity, Macular Thickness, and Vision Related Quality of Life Post Laser Photocoagulation among Diabetic Macular Edema Patients

Abstract - Objectives: This study aims to assess the treatment satisfaction post laser photocoagulation among diabetic macular edema (DME) patients by evaluating the visual function (visual acuity and contrast sensitivity), macular thickness and vision related quality of life (QoL) score post laser photocoagulation. Methods: DME patients were selected and categorised into mild, moderate, and severe groups, All patients underwent focal or grid laser photocoagulation. The visual acuity, contrast sensitivity, macular thickness, and vision related QoL scoring were performed at baseline and at 3 months post focal or grid laser photocoagulation. Vision related QoL scores were measured using National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25). Results: A total of 61 patients (111 eyes) with DME were included in this study (mild DME, 40 eyes; moderate DME, 35 eyes; severe DME, 36 eyes). At 3 months post laser photocoagulation, moderate and severe DME showed significantly improved in the mean visual acuity (p<0.001 and p=0.047, respectively). There was no significant difference of mean contrast sensitivity between baseline and post laser photocoagulation in each group of DME. The mean macular thickness was significantly reduced in mild DME (p<0.001) and moderate DME (p=0.049). The mean vision related QoL score was significantly increased in moderate DME (p=0.002) and severe DME (p=0.038). Conclusion: Moderate and severe DME demonstrated a significant impact post laser photocoagulation treatment with a significant increase of vision related QoL score which was consistent with significant improvement of visual acuity.

Keywords – Diabetic macular edema, contrast sensitivity, laser photocoagulation, macular thickness, vision related quality of life, visual acuity

1. INTRODUCTION

Diabetic macular edema (DME) is one of the main causes of visual loss in over 75% of diabetic patients [1]. It is defined as an increase in macular thickness due to breakdown of blood retinal barrier causing accumulation of fluid in the intra-retinal layers. All diabetic patients are at risk to develop DME which is one of the common microvascular complications that can occur at any stage of diabetic retinopathy.

Early detection of retinal changes is important in preventing visual loss. Evaluation of maculopathy can be done by using the slit lamp, fundus photography and fundus fluorescein angiography (FFA) [2]. Some of the methods are subjective and observer dependent. The fundus fluorescein is an invasive procedure and sometimes will give unpleasant side effects. These instruments are relatively insensitive to small changes in the retinal thickness.

Recently, newer imaging techniques have been introduced to evaluate the retinal thickness such as optical coherence tomography (OCT), retinal thickness analysis and Heidelberg retinal tomography (HRT) [3]. OCT is used to quantify macular edema and has been introduce gives a better quantitative estimation of retinal thickness [4].

Currently, anti-vascular endothelial growth factor (VEGF) is the standard treatment for DME especially DME with central involvement. Laser photocoagulation had been the mainstay of treatment for DME for almost for the past 35 vears. Early Treatment Diabetic Retinopathy Study (ETDRS) showed an approximate 50% reduction in the rate of moderate vision loss at 3 years following laser photocoagulation compared to no treatment [5]. Laser photocoagulation is used in conjunction with anti-VEGF therapy, typically when DME persists and is not continuing to improve after at least 6 months of monthly injections of anti-VEGF therapy. It is still a preferred therapy for DME in selected patients especially in the developing countries, as its lower cost and less intensive management requirements compared to anti-VEGF. Focal laser photocoagulation for clinically significant macular edema (CSME) in diabetics helps in improving the contrast sensitivity and stabilizes the visual acuity [6].

Contrast sensitivity can be used to evaluate the patient response to the initiation of therapy or to a change in therapy. Impairment of contrast sensitivity in diabetic patients is probably due to capillary drop out in the retina. It is also affected by other ocular diseases such as dry eye, glaucoma, myopia, optic neuritis, post cataract operation, radial keratotomy, and photorefractive keratectomy [7].

DME patient experience a decrease quality of life (QoL) [8]. The QoL is a broad concept to measure patient's perspectives included the physical wellbeing, functional ability, emotional and social wellbeing by using questionnaires. Photocoagulation for DME has a beneficial effect on patients' subjective perception of visual function. The use of vision-targeted health status questionnaires in conjunction with the clinical examination appears to provide a more comprehensive overview of individuals' daily wellbeing following laser treatment [9].

The aim of this study is to assess the treatment satisfaction post laser photocoagulation among DME patients by evaluating the visual function (visual acuity and contrast sensitivity), macular thickness and vision related QoL score post laser photocoagulation.

2. METHODS Study design This was a prospective study. The study period was from April 2009 to March 2011. Patients were recruited using convenience sampling. Ethical approval was obtained from the Research and Ethical Committee, School of Medical Sciences, Universiti Sains Malaysia (Reference no. 217.3.(14)). The study was conducted in accordance with the tenets of the Declaration of Helsinki and the Malaysian Guidelines for Good Clinical Practice. Written informed consent was obtained from all patients.

Participants

Sample size was calculated using 'Power & Sample' software. It was calculated based on changes in visual acuity [10], contrast sensitivity [10], macular thickness [11], and vision related QoL score [8] preand post-laser photocoagulation in DME. The minimum sample size that acquired for this study was 104 eyes (35) eyes for each group of DME). All diabetic patients presented with diabetic maculopathy with clear media were screened for DME. Diabetic patient with evidence of other causes of macular edema such as age-related macular degeneration or due to retinal vein occlusion were excluded from the study. Other ocular disorders that affect the contrast sensitivity assessment such as glaucoma or optic nerve disorder were also excluded. DME patient that has previous history of laser photocoagulation therapy, intravitreal anti-VEGF injection, intravitreal or periocular steroid injection or history of intraocular surgery were excluded from the study. DME patients with poor diabetic control (HbA1c more than 12 %) were also excluded.

Classification of DME

Eyes with DME that fulfilled the selection criteria were grouped into the severity of DME; mild, moderate, and severe accordingly following the International Clinical Disease Severity Grading Scale for Diabetic Retinopathy and Diabetic Macular Edema [12] with modification. In this study, DME was grouped into mild, moderate, and severe with guided from FFA. Presence of macular edema is characterised by the presence of microaneurysm (focal type of macular edema) or leakage from extensive area of generalised breakdown retinal capillaries throughout the posterior pole (diffuse type of macular edema) by FFA. The fundus captured image was divided into nine ETDRS sectors of macular area (Figure 1) with 1 mm, 3 mm, and 6 mm circle at central fovea. Any macular edema seen within 1 mm circle at central macular was termed as severe DME. Macular edema seen between 1 mm and 3 mm circles (in any of four quadrants) was termed as moderate DME. Macular edema seen between 3 mm and 6 mm circles (in any of four quadrants) was considered as mild form of DME (Figure 1). Then, the patient was given an appointment for baseline parameter evaluation within a week.

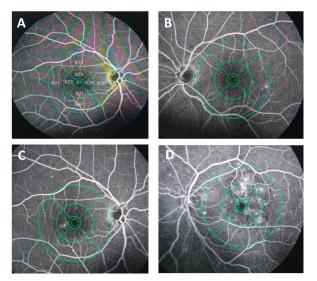


Figure 1. Nine Early Treatment Diabetic Retinopathy Study (ETDRS) sectors of macular area (A). Classification diabetic macular edema (DME) with guided fundus fluorescein angiography showed mild DME (B), moderate DME (C) and severe DME (D)

Ocular examination

Ocular parameters for visual acuity, contrast sensitivity, macular thickness, and vision related questionnaire for QoL scoring were performed before and at 3 months after commenced the laser photocoagulation (focal/grid) therapy for DME. For visual acuity assessment, since distance visual acuity is the most frequent test used in clinical practice and research, therefore near visual acuity was not assessed in this study. The term visual acuity in this study is referred to the distance visual acuity. The visual acuity was done using Snellen chart and the Snellen values were converted to logarithm of the minimum angle of resolution (logMAR) notation. Subjective refraction was performed by an identified optometrist before proceeding to contrast sensitivity assessment. Best corrected visual acuity (BCVA) is required for contrast sensitivity assessment. Only logMAR BCVA was taken for analysis of visual acuity in this study. CSV 1000 chart was used to record the contrast sensitivity. The patient was instructed to read the chart from a distance of 8 feet with their BCVA. Only one eye was tested at one time for 3, 6, 12 and 18 cycle/degree. The reading was plotted to the Vector Vision contrast sensitivity chart and converted to log contrast sensitivity. The procedure was done by an identified optometrist.

Macular thickness was taken using the OCT (Stratus OCT, Carl Zeiss Meditec). The selected eyes were dilated before the measurement. Numeric values in each of the nine sectors were obtained and documented as mean global macular thickness. OCT examination was done by a trained medical technician.

Vision-related QoL score was held in person trained research assistant using а bv questionnaire National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25). The NEI VFQ-25 consists of 25 questions and are divided into 3 main domains include general health, quality of vision and vision related QoL. The respond from the patient was calculated follows the scoring key and each item was converted to 100 points scale; 100 being the highest score (better QoL) and 0 being the lowest score (poor QoL). Each question has its own specific subscales; therefore the average was calculated as a score for each subscale. The vision related QoL score was assessed as one person. If the two eyes had unequal grouping of DME, the eye with worst DME was selected as the status of DME for that patient.

Laser photocoagulation procedure

Laser photocoagulation procedure was performed after completion the baseline measurement using Carl Zeiss Visulas 532S laser system. A standard setting spot size of 100 µm and duration of 100 ms with titrating of laser power were used. The laser burn was light gray in colour with 500 µm area around the fovea was spared. A localized macular edema with microanuerysm received focal laser. The grid laser was applied around the thickening area with spacing of one burn area. The procedure was done by one identified ophthalmologist to eliminate bias. The guidelines for laser adapted from ETDRS. The patients were given 3 months follow-up post laser photocoagulation procedure to repeat the ocular parameters.

Statistical analysis

All the statistical analysis and data entry were done using Statistical Package for Social

Sciences (SPSS Inc) software version 18.0. Comparison of visual acuity, contrast sensitivity, macular thickness and vision-related QoL score between baseline and at 3 months post laser photocoagulation in mild, moderate, and severe DME were analysed using paired t-test.

3. RESULTS Demographic data

A total of 61 patients (111 eyes) with DME were recruited from April 2009 till March 2011. The mean age was 56.7 ± 7.24 years in all groups

with minimum age of 30 years and maximum age of 70 years respectively. There were 59 (96.7%) patients of Malay ethnic and non-Malays were 2 (3.3%) patients which were Chinese. Thirty of them (49.2%) were male patients and 31 (50.8%) patients were female. Out of 111 eyes of DME, 40 (36.0%) eyes were mild DME, 35 (31.5%) eyes were moderate DME and 36 (32.4%) eyes in severe DME group. The distribution of demographic data and grading of DME is shown in Table 1.

 Table 1. Demographic data and grading of DME

Parameter	Number	Percentage (%)	
DME patients (n = 61 patients	s)		
Age (years) Race	56.7 ±7.24*	-	
Malay	59	96.7%	
Non-Malay	2	3.3%	
Sex			
Male	30	49.2%	
Female	31	50.8%	
Grading of DME (n = 111 eye	es)		
Mild	40	36.0%	
Moderate	35	31.5%	
Severe	36	32.4%	

* Mean ± SD

Abbreviation: DME, diabetic macular edema

Comparison of visual acuity, contrast sensitivity, macular thickness, and vision related QoL score between baseline and post laser photocoagulation among DME

There were significant differences of mean logMAR BCVA between baseline and post laser photocoagulation in moderate and severe DME. The mean logMAR BCVA of moderate and severe DME was significantly improved at 3 months post laser photocoagulation compared to baseline (p < 0.001 and p = 0.047 respectively) (Table 2). The contrast sensitivity was analysed based on the number of cycle/degree (3 cycle, 6 cycle, 12 cycle and 18 cycle). Although the mean of all the cycles of contrast sensitivity was at increased 3 months post laser photocoagulation compared to baseline in all groups of DME, but there were no significant differences of mean for all the cycles of contrast sensitivity in all groups of DME (Table 2). Mean macular thickness was reduced at 3 months post laser photocoagulation compared to baseline in

mild and moderate DME (p<0.001 and p=0.049 respectively (Table 2). Although the mean total score vision-related QoL was increased at 3 months post laser photocoagulation compared to baseline in all groups of DME, but only the moderate and severe groups of DME showed significant different of mean score for vision-related QoL (p=0.038 and p=0.002 respectively) (Table 2).

4. DISCUSSION

DME is known to be the leading cause of visual impairment in diabetic retinopathy patients [13,14]. Blindness is known to be the sequelae of the diabetic maculopathy or proliferative diabetic retinopathy. In present study, in view of limited funding for anti-VEGF, laser photocoagulation is the choice of treatment for all stages of DME. Instead of giving laser to the CSME according to ETDRS, the patients were grouped according to the severity of DME, and focal/grid laser was applied to the localised area of retinal thickening.

	At baseline	At 3 months post laser Mean (SD)	Mean diff	p value
	Mean (SD)			
LogMAR BCVA (n	= 111 eyes)			
Mild DME Moderate DME Severe DME	0.18 (0.19) 0.22 (0.19) 0.55 (0.33)	0.16 (0.13) 0.15 (0.20) 0.46 (0.35)	0.03 (0.15) 0.07 (0.09) 0.08 (0.24)	0.269 <0.001 0.047
Contrast Sensitiv	ity 3 cycle/degree (n =	= 111 eyes)		
Mild DME Moderate DME Severe DME	0.82 (0.18) 0.81 (0.15) 0.62 (0.21)	1.04 (1.14) 0.83 (0.14) 0.68 (0.24)	-1.21 (39) -1.17 (34) -1.90 (35)	0.235 0.251 0.066
Contrast Sensitiv	ity 6 cycle/degree (n =	= 111 eyes)		
Mild DME Moderate DME Severe DME	0.82 (0.16) 0.81 (0.15) 0.69 (0.17)	0.86 (0.16) 0.83 (0.14) 0.82 (0.74)	-1.30 (39) 0.84 (34) -1.13 (35)	0.200 0.404 0.266
Contrast Sensitiv	ity 12 cycle/degree (n	= 111 eyes)		
Mild DME Moderate DME Severe DME	0.84 (0.24) 0.84 (0.26) 0.57 (0.23)	0.90 (0.23) 0.87 (0.23) 0.61 (0.27)	-1.78 (39) -0.96 (34) -1.08 (35)	0.820 0.343 0.287
Contrast Sensitiv	ity 18 cycle/degree (n	= 111 eyes)		
Mild DME Moderate DME Severe DME	0.83 (0.38) 0.78 (0.34) 0.48 (0.37)	0.89 (0.35) 0.82 (0.30) 0.50 (0.41)	-1.28 (39) -0.61 (34) -0.34 (35)	0.209 0.548 0.733
Macular thickness	s (μm) (n = 111 eyes)			
Mild DME Moderate DME Severe DME	327.43 (37.40) 362.29 (52.88) 389.94 (105.94)	305.27 (22.29) 345.69 (50.86) 389.06 (115.61)	22.15 (34.60) 16.60 (48.94) 0.88 (82.93)	<0.001 0.049 0.949
QoL score (n = 61	patients)			
Mild DME Moderate DME Severe DME	81.55 (15.39) 71.19 (12.65) 65.10 (18.23)	82.40 (16.26) 73.65 (13.88) 68.08 (18.04)	-0.760 (17) -2.293 (18) -3.602 (23)	0.458 0.038 0.002

 Table 2. Comparison of visual acuity (logMAR BCVA), contrast sensitivity, macular thickness, and vision related

 QoL score at baseline and post laser photocoagulation in each group

Paired t test, significant p<0.05

Abbreviation: LogMAR, logarithm of the minimum angle of resolution; BCVA, best corrected visual acuity; DME, diabetic macular edema; QoL, quality of life

Pamu et al [15] reported a study of 30 eyes with non-centre involved DME underwent focal/grid laser photocoagulation at 6 months follow up found that BCVA was stabilized in 63% improved by 26% and decreased by 10%. They also found that contrast sensitivity was also

significantly improved at 3- and 6-months followup. They concluded that timely treatment of DME with laser photocoagulation prevents further dysfunction of retina and lead to improvement in vision and QoL. The effectiveness of laser therapy in DME was verified with a stability of visual acuity for at least 4 months [16]. Retreatment is indicated for new lesions or recurrent leakage in DME up to 3 to 4 months after the initial laser therapy [16,17]. In our study, we evaluated the outcome at 3 months post laser photocoagulation. Therefore, re-treatment can be performed if indicated.

In this current study, a total of 61 patients (111 eyes) were recruited. Forty eyes in mild DME, 35 eyes in moderate DME and 36 eyes in severe DME were included in the study which is well distributed. The age, gender and race in all groups were comparable. Total of 59 patients (96.7%) were Malays which are the majority population in Kelantan. Therefore, Malay's patients dominated the study population and only two patients were Chinese included in this study.

DME is a clinical diagnosis. ETDRS classified DME into CSME and non-CSME based on the proximity of visible retinal thickening or hard exudates to the fovea [18]. The International Council of Ophthalmology (ICO) classified DME into center-involved and non-center-involved DME based on clinical OCT findings [18]. In this current study, DME was classified based on International Clinical Disease Severity Grading Scale for Diabetic Retinopathy and Diabetic Macular Edema [12] with modification. ETDRS nine sectors of macular area was applied to determine accurately the distance of macular edema from the centre of fovea. In addition, FFA was performed to locate focal lesions such as microaneurysm or focal leakage that not obvious on clinical examination.

In mild DME, the baseline logMAR BCVA was the best among the other group of DME. The mean logMAR BCVA was 0.18 ± 0.19 at baseline and slight improvement to 0.16 ± 0.13 at 3 months post laser photocoagulation. However, it was not significant. In mild DME, the areas of involvement were located at extrafoveal region. There was no impact on the visual acuity and contrast sensitivity in patient presented with extrafoveal localised macular edema [19]. Deterioration of the visual acuity is observed when there is fovea involvement macular edema.

We found that the baseline logMAR BCVA in moderate and severe DME groups were 0.22 \pm

0.19 and 0.55 ± 0.33 respectively which was worst in severe DME. There was significant improvement LogMAR BCVA in moderate and DME at 3 months severe post laser photocoagulation (p < 0.001 and p = 0.047respectively). In contrast to mild DME, the area of involvement in severe DME was located at the foveal region. Laser treatment will reduce edema at foveal region and resulted in improvement of vision. Although there was no edema at foveal region in moderate DME, we postulated that the effect of laser therapy in moderate DME will not only reduce the edema surrounding the foveal but also has the effect at foveal region.

In RESTORE clinical trial [20], the mean average change in BCVA showed improvement of 0.8 from baseline through 12 months follow up for laser monotherapy in DME. The aim of RESTORE was to demonstrate the superiority of ranibizumab as a monotherapy or combined with laser or laser alone. The BCVA letter score >73 (20/40-Snellen equivalent) in laser monotherapy had improvement from 15.3 % at baseline versus 23.6 % at month 12.

There were studies reported that there was minimal or no improvement of the visual acuity after laser treatment [21,22]. Greenstein et al [21] reported only two out of nine patients with showed DME intermediate а significant improvement in visual acuity after laser therapy. The other patients were consistent with a stabilization of visual acuity. Masoud et al [22] conducted a randomised, three-arm clinical trial to compare the intravitreal bevacizumab alone or combined with triamcinolone versus macular photocoagulation as a primary treatment of DME. They found that the mean corrected visual acuity at 6 weeks and 12 weeks showed deterioration in the laser group compared to baseline.

Diffuse DME tends to have poor visual acuity even post laser photocoagulation. The edema map of the severe DME group showed involvement of the fovea region and tend to be diffuse type which is difficult to treat by laser photocoagulation. There were 61% of diffuse DME remained unchanged and 24% worsening of visual acuity post grid laser photocoagulation [23].

OCT has been used in evaluation, diagnosis, and follow-up of DME [24,25]. The mean edema index using the scanning laser tomography showed reduction approximate to baseline values after 12 weeks of laser therapy [19]. Hudson et al [19] found that not all patients showed the correlation of the mean edema index with visual function.

In our study, we found that there was significant reduction of macular thickness in mild and moderate DME group at 3 months post laser photocoagulation. Although, there was reduction of macular thickness at 3 months post laser photocoagulation, but the value of macular thickness was still above the normal value (more than 280 µm). There are few factors that cause persistent or poor reduction of macular thickness post laser treatment such as presence of epiretinal membrane, vitreo-retinal traction, hard exudates or hyperreflective intraretinal foci, or subretinal fluid [26]. Reduction of macular thickness will produce a better visual acuity. Only moderate DME showed a good relationship between visual acuity and macular thickness in which there was a significant improvement of visual acuity with significant reduction of macular thickness. The severe DME group had improvement of visual acuity but there was no significant reduction of macular thickness. We postulated that severe DME probably had diffuse type edema that became refractory type of DME. Beside persistent or poor reduction of macular thickness, disorganization of the inner retinal layers also can lead to decrease visual functions [26].

Contrast sensitivity is one of the visual functions that had been measured to determine the effectiveness of the procedure and diagnosis of early or advanced diabetic retinopathy. In current study, we found that the mean log contrast sensitivity at 3, 6, 12 and 18 cycle/degree was reduced in all DME groups at baseline in comparison with normal population. There was no significant difference in contrast sensitivity measurement between baseline and 3 months post laser treatment in each group. Similarly, Gabriel et al [27] demonstrated that there was an impairment of contrast sensitivity in diabetic patient even without retinopathy. They found that the patients with good visual acuity with normal fundus examination and normal OCT noted to have impaired mesopic contrast sensitivity. The reduction of contrast sensitivity in diabetic patient was hypotheses due to ischemia of the retinal ganglion cell that causing expansion of foveal avascular zone and retinal hypoxia.

In contrast, there were few studies showed improvement of contrast sensitivity and stabilization of visual acuity post laser photocoagulation for CSME [1,6]. Furthermore,

Farahvash et al [6] evaluated the contrast sensitivity after three modalities of treatment for CSME and demonstrated that there was significant improvement of contrast sensitivity in patient treated with laser and the effect was better in the group treated with combined laser and anti-VEGF.

There were increasing trend of assessing visual function using patient's self-assessed visual function over the past 20 years which obtained by asking questions, self-administered questionnaires, or an interview. Questionnaire is known as one of the tools to measure the outcome of diabetic retinopathy which is humanistic in nature. In this current study, NEI VFQ-25 was used to assess the vision-related QoL. The original version of NEI VFQ-25 has been translated into Malay version in order to prevent language barrier.

Vision impairment related with diabetic retinopathy or macular edema may give impact on patient's functioning, physical, psychosocial, and financial wellbeing. Davidov et al [28] found that physical and mental component of health related QoL were influenced by the variables such as diabetic retinopathy severity grade, macular edema, visual acuity, and co-morbidities. Hariprasad et al [8] concluded that there was significant decreased of vision related QoL in type 2 diabetes patients with macular edema compared to those with type 1 diabetic patient with retinopathy, glaucoma, and cataract.

We evaluated the vision-related QoL using NEI VFQ-25 to determine the impact of laser in various severity of DME. There were significantly improved of vision related QoL score at 3 months post laser photocoagulation in moderate and severe groups of DME. Even though the mild DME group did not show significant improvement, but the highest vision related QoL score was seen in this group. In relation to the visual acuity, there was presence of relationship between visual acuity and the score of vision related QoL in moderate and severe DME. In these DME groups, the patients with significant visual acuity improvement had significant gain of vision related at 3 months QoL score post laser photocoagulation.

Tranos et al. [9] demonstrated the improvement in almost all aspects of visual function in patients with DME post laser treatment. Their patients underwent assessment QoL by using VFQ-25 at baseline and 3 months post intervention. Mitchell et al [20] also reported that DME patients treated either with anti-VEGF

as monotherapy or combined with laser showed to have gain in VFQ-25 scores.

The RESTORE study [20] used the NEI VFQ-25 to assess the impact of treatment on health related QoL for DME patient. It showed progressive and sustained improvement in health related QoL that associated with the gains in visual acuity after the interventions. Only 24% of patients with laser as monotherapy reported to have excellent to good vision compared to 20% at baseline.

The macular edema has the negative effect on health related QoL since it affects the binocular vision. The severity of the diabetic retinopathy had indirect effect on the health related QoL through visual acuity impairment and macular edema which affected the mental and physical components [28]. Other variables, the patient's co-morbidities also inversely associated with QoL. In our study, we found that the macular thickness in severe DME group at baseline was the thickest among the group of DME with only slight reduction at 3 months post laser treatment. It correlates with the score of the QoL which showed the lowest scores in this group.

Recently, many studies evaluated the other treatment modalities such as intravitreal anti-VEGF and steroid, alone or combination with laser in treating DME [6,20,22,29,30]. The DRCRnet study, a randomized, multicenter clinical study showed 20% of the post laser patient demonstrated worsening of visual acuity [29]. A few studies also concluded that the combined treatment (anti-VEGF and laser or IVTA and laser) showed superior result in visual acuity in comparison with laser as monotherapy [6,20,22]. Unfortunately, the patients with chronic DME did not show benefit from intravitreal triamcinolone injection over conventional laser therapy [30].

This current study suggested that laser photocoagulation is effective in treating DME patients of moderate severity, while there was no significant improvement in visual functions in eyes with mild DME. Severe DME receiving laser photocoagulation, suggesting the need for combined treatment with other pharmacological agents such anti-VEGF or steroids.

This study does have some limitations. Visual acuity is one of the visual function measurements that commonly used. In view of distance visual acuity is the most frequent test used in clinical practice and research, near visual acuity was not assessed in this study. We strongly recommend evaluating near vision and other visual functions such as dark adaptation, visual field, and colour perception in future study. Beside visual strongly functions. we also recommend evaluating others ocular demographic data such as intraocular pressure, axial length, corneal thickness, endothelial count that has related effect to laser photocoagulation for more complete ocular assessment. Another limitation of this study is the lack of data after 3 months follow-up period. A longer follow-up period might be needed to look for the long-term effect of visual function post laser photocoagulation among DME patients.

5. CONCLUSION

Moderate and severe DME demonstrated a significant impact post laser photocoagulation treatment with a significant increase of vision related QoL score which was consistent with significant improvement of visual acuity. Moderate DME showed more impact post laser photocoagulation than severe DME which was demonstrated not only improvement in vision related QoL but also improvement in structural changes with significant reduction of macular thickness. However, there was no improvement of contrast sensitivity post laser photocoagulation treatment. Longer follow-up is recommended to look the long-term effect of laser treatment on visual functions.

REFERENCES

- [1] Talwar D, Sharma N, Pai A, Azad RV, Kohli A, Virdi PS. Contrast sensitivity following focal laser photocoagulation in clinically significant macular oedema due to diabetic retinopathy. *Clin Exp Ophthalmol.* 2001; 29(1): 17-21. doi: 10.1046/j.1442-9071.2001.00361.x.
- [2] Kisilevsky M, Hudson KMC, Flanagan JG, Nrusimhadevara RK, Guan K, Wong T, et al. Agreement of Heidelberg Retinal Tomography II macula oedema module with fundus biomicroscopy in diabetic maculopathy. Arch Ophthalmol. 2006; 124 (3): 337-342. doi: 10.1001/archopht.124.3.337.
- [3] Goebel W, Kretzchmar-Gross T. Retinal thickness in diabetic retinopathy: A study using optical coherence tomography (OCT). *Retinal.* 2002; 22(6): 759-767. doi: 10.1097/00006982-200212000-00012.
- [4] Knight ORJ, Chang RT, Feuer WJ, Budenz DL. Comparison of retinal nerve fiber layer measurements using time domain and spectral domain optical coherent tomography. *Ophthalmology*. 2009; 116(7): 1271-1277. doi: 10.1016/j.ophtha.2008.12.032.
- [5] Wenick AS, Bressler NM. Diabetic Macular Edema: Current and Emerging Therapies. *Middle East Afr J Ophthalmol.* 2012; 19(1): 4-12. Doi: 10.4103/0974-9233.92110
- [6] Farahvash MS, Aslani A, Faghihi H, Ghaffari E, Mirshahi A, Faghihi S, et al. The comparison of contrast sensitivity after 3 different treatment modalities for clinically

significant macular edema. *Iran J Ophthalmol.* 2010; 22(4): 66-72.

- [7] Puell MC, Benitez-Del-Castillo JM, Martinez-De-La-Casa J, Sanchez-Ramos C, Vico E, Perez-Carrasco MJ, et al. Contrast sensitivity and disability glare in patients with dry eyes. Acta Ophthalmol Scand. 2006; 84(4): 527-531. doi: 10.1111/j.1600-0420.2006.00671.x.
- [8] Hariprasad SM, Mieler WF, Grassi M, Green JL, Jager RD, Miller L. Vision related quality of life in patient with diabetic macular oedema. *Br J Ophthalmol.* 2008; 92(1): 89-92. doi: 10.1136/bjo.2007.122416.
- [9] Tranos PG, Topouzis F, Stangos NT, Dimitrakos S, Economidis P, Harris M, et al. Effect of laser photocoagulation treatment for diabetic macular oedema on patient's vision-related quality of life. *Curr Eye Res.* 2004; 29(1): 41-49. doi: 10.1080/02713680490513191.
- [10] Bandello F, Polito A, Del Barello M, Zamella N, Isola M. "Light" versus "classic" laser treatment for clinically significant diabetic macular oedema. *Br J Ophthalmol.* 2005; 89(7): 864-870. doi: 10.1136/bjo.2004.051060.
- [11] Ang A, Tong L, Vernon SA. Improvement of reproducibility of macular volume measurement using the Heidelberg retinal tomography. *Br J Ophthalmol.* 2000; 84(10): 1194-1197. doi: 10.1136/bjo.84.10.1194.
- [12] Wilkinson CP, Ferris 3rd FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular oedema disease severity scales. *Ophthalmology*. 2003; 110(9): 1677-1682. doi: 10.1016/S0161-6420(03)00475-5.
- [13] Romero-Aroca P. Managing diabetic macular edema: the leading cause of diabetes blindness. *World J Diabetes*. 2011; 2(6): 98-104. doi: 10.4239/wjd.v2.i6.98.
- [14] Bhagat N, Grigorian RA, Tutela A, Zarbin M A. Diabetic macula edema: Pathogenesis and treatment. *Surv Ophthalmol.* 2009; 54(1): 1-32. doi: 10.1016/j.survophthal.2008.10.001.
- [15] Pamu NJ, Rao VJ, Chandana-Priyanka S. Effect of laser photocoagulation on contrast sensitivity, visual acuity and colour vision in patients of diabetic macular edema. *Int J Adv Res.* 2019; 7(2): 801-805. doi:10.21474/IJAR01/8548.
- [16] Romero-Aroca P, Reyes-Torres J, Baget-Bernaldiz M, Blasco-Suñe C. Laser treatment for diabetic macular edema in the 21st Century. *Curr Diabetes Rev.* 2014;10: 100-112.
- [17] González-Cortés JH. Treatment of Diabetic Macular Edema (DME): Shifting paradigms. *Medicina Universitaria*. 2015;17(69): 243-247.
- [18] Hui VWK, Szeto SKH, Tang F, Yang D, Chen H, Lai TYY, et al. Optical coherence tomography classification systems for diabetic macular edema and their associations with visual outcome and treatment responses – an updated review. Asia Pac J Ophthalmol (Phila). 2022;11: 247–257.
- [19] Hudson C, Flanagan JG, Turner GS, Chen HC, Young LB, McLeod D. Correlation of a scanning laser derived oedema index and visual function following grid laser treatment for diabetic macular oedema. *Br J Ophthalmol.* 2003; 87(4): 455-461. doi: 10.1136/bjo.87.4.455.

- [20] Mitchell P, Bandello F, Schmidt-Erfurth U, Lang GE, Massin P, Schlingemann RO, et al. The RESTORE Study. ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. *Ophthalmology.* 2011; 118(4): 615-625. doi: 10.1016/j.ophtha.2011.01.031.
- [21] Greenstein VC, Chen H, Hood DC, Holopigian K, Seiple W, Carr RE. Retinal function in diabetic macular edema after focal laser photocoagulation. *Invest Ophthalmol Vis Sci.* 2000; 41(11): 3655-3664.
- [22] Soheilian M, Ramezani A, Bijanzadeh B, Yaseri M, Ahmadieh H, Dehghan MH, et al. Intravitreal bevacizumab (avastin) injection alone or combined with triamcinolone versus macular photocoagulation as a primary treatment of diabetic macular edema. *Retina*. 2007; 27(9): 1187-1195. doi: 10.1097/IAE.0b013e31815ec261.
- [23] Chan WC, Tsai SH, Wu AC, Chen Lj, Lai CC. Current Treatments of Diabetic Macular Edema. *Int J Gerontol.* 2011; 5(4): 183-188. doi.Org/10.1016/J.ljge.2011.09.013.
- [24] Degenring RF, Aschmoneit I, Kamppeter B, Budde WW, Jonas JB. Optical coherence tomography and confocal scanning laser tomography for assessment of macular edema. Am J Ophthalmol. 2004; 138(3): 354-361. doi: 10.1016/j.ajo.2004.04.021.
- [25] Yang CS, Cheng CY, Lee FL, Hsu WM, Liu JH. Quantitative assessment of retinal thickness in diabetic patients with and without clinically significant macular edema using optical coherence tomography. *Acta Ophthalmol Scand.* 2001; 79(3): 266-270. doi: 10.1034/j.1600-0420.2001.790311.x.
- [26] Panozzo G, Cicinelli MV, Augustin AJ, Parodi MB, Cunha-Vaz J, Guarnaccia G, et al. An optical coherence tomography-based grading of diabetic maculopathy proposed by an international expert panel: The European School for Advanced Studies in Ophthalmology classification. *Eur J Ophthalmol.* 2020;30(1): 8–18. doi: 10.1177/1120672119880394
- [27] Katz G, Levkovitch-Verbin H, Treister G, Belkin M, Ilany J, Polat U. Mesopic foveal contrast sensitivity is impaired in diabetic patients without retinopathy. *Graefes Arch Clin Exp Ophthalmol.* 2010; 248(12): 1699-1703. doi: 10.1007/s00417-010-1413-y.
- [28] Davidov E, Breitscheidel L, Clouth J, Reips M, Happich M. Diabetic retinopathy and health- related quality of life. *Graefes Arch Clin Exp Ophthalmol.* 2009; 247(2): 267-272. doi: 10.1007/s00417-008-0960-y.
- [29] Diabetic Retinopathy Clinical Research Network Writing Committee, Haller JA, Qin H, Apte RS, Beck RR, Bressler NM, et al. Vitrectomy outcomes in eyes with diabetic macular edema and vitreomacular traction. *Ophthalmology.* 2008; 117(6): 1087-1093. doi: 10.1016/j.ophtha.2009.10.040.
- [30] Ockrim ZK, Sivaprasad S, Falk S, Roghani S, Bunce C, Gregor Z, et al. Intravitreal triamcinolone versus laser photocoagulation for persistent diabetic macular oedema. Br J Ophthalmol. 2008; 92(6): 795-799. doi: 10.1136/bjo.2007.131771.