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Effect of panretinal photocoagulation on retinal nerve fiber layer thickness and vision-related quality of life in proliferative diabetic retinopathy patients

***Abstract*—**The purpose of this study is to evaluate the retinal nerve fiber layer (RNFL) thickness and vision-related quality of life (VRQoL) in type 2 diabetes mellitus (T2DM) patients with proliferative diabetic retinopathy (PDR) following panretinal photocoagulation (PRP). A prospective cohort study was conducted from June 2012 until December 2013. Visual acuity was evaluated using Snellen chart (converted to LogMAR decimal notation), RNFL thickness using optical coherence tomography and VRQoL using Visual Function Questionnaire-25 (VFQ-25) before and at three months after completed PRP. A total of 44 PDR patients were enrolled into this study. There was significant reduction of mean visual acuity at three months post PRP ($p < 0.001$). Both mean global RNFL thickness and mean composite score of VFQ-25 showed significant reduction at three months post PRP ($p < 0.001$ and $p < 0.001$ respectively). There was significant fair negative correlation between VFQ-25 composite score and LogMAR visual acuity post PRP ($r = -0.425$, $p = 0.004$). PRP was associated with reduction of RNFL thickness and VFQ-25 composite score in T2DM patient with PDR at three months post PRP. Longer duration of follow-up is recommended to look for the long-term effect of VRQoL from laser therapy.

***Keywords* — Panretinal photocoagulation, proliferative diabetic retinopathy, retinal nerve fiber layer, vision-related quality of life**

1 INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of visual impairment and blindness in developed countries, mainly due to macular oedema and proliferative diabetic retinopathy (PDR) [1-3]. PDR is characterised by the presence of neovascularisations, either on the disc or elsewhere on the retina. About 10% of people after 15 years of diabetes mellitus (DM) are likely to develop severe visual handicap due to these complications [4,5]. Laser therapy had brought significant benefits in stabilizing DR. Panretinal photocoagulation (PRP) is used to treat PDR to prevent visual loss from the consequences of DR [6]. PRP demonstrated 50-60% reduction in the rate of severe visual loss after a five-year follow-up period [7,8].

Woodcock et al [9] reported that there are consequences after laser therapy in DR such as adjusting to dim and bright lighting, sorting dark colours, judging distance, negotiating stairs or undertaking athletic activities, which will influence the vision-related quality of life (VRQoL). The laser therapy itself destroys retinal tissue and cause thinning of retinal nerve fiber layer (RNFL) thickness; therefore, multiple treatments of laser therapy tend to have the effect of increasing visual impairment [10].

Several questionnaires have been developed to assess the VRQoL such as Short-Form Health Survey (SF-12) questionnaire, Retinopathy-dependant Quality of Life questionnaire (RetDQoL), Medical Outcome Study Short Form 36 (SF-36) and National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25 or VFQ-25). The VFQ-25 was developed by the National Eye Institute [11]. It was developed from patient focus groups representing a diverse set of visual conditions and can be used for developmental conditions such as cataract, glaucoma, age-related macular degeneration, and DR, as well as for other conditions as diverse as

corneal diseases and vascular occlusions of the retina. The advantage of VFQ-25 is that it is specific for the patient with vision problems.

The purpose of this study is to evaluate the peripapillary RNFL thickness and to assess the VRQoL among type 2 diabetes mellitus (T2DM) with PDR that treated with PRP. The outcome of VRQoL post PRP in this study will help us to understand the problem that may arise in PDR patients undergoing PRP.

2 METHODS

This study design was a prospective cohort study and was conducted from June 2012 until December 2013. The study population were all T2DM patients with PDR. Newly diagnosed PDR patient aged 40 – 60 years old, and without ocular media opacity were included in this study. Patients with vitreous or pre-retinal haemorrhage, retinal fibrosis or clinically significant macular oedema, history of intravitreal injection of medication such as triamcinolone or anti-vascular endothelial growth factor (VEGF), refractive error of ± 2 Diopter (D), and pseudophakic patients were excluded from the study. The study was approved by local Research and Ethical Committee (USMKK/PPP/JEPeM [230.3.(06)] and-adhered to the tenets of the Declaration of Helsinki. A written informed consent was taken from the patients' prior data collection.

The assessment of visual acuity was done using Snellen chart and followed by subjective refraction. Visual acuity in the Snellen fraction was converted to Logarithm of the minimum angle of resolution (LogMAR) decimal notation. Detailed ocular examination was done by the primary investigator. Only one eye with PDR was selected for each patient for measurement of RNFL thickness. If both eyes have PDR but one eye has ocular media opacity, the eye without ocular media opacity was chosen. If both eyes had similar findings, then the right eye was chosen.

The RNFL thickness was measured using Cirrus HD-OCT machine (Carl Zeiss Meditec, Inc., Dublin, CA, USA) by one identified trained medical personnel. A good image surrounding the optic nerve head was obtained. The cut off point for the signal strength taken for this study was ≥ 6/10. The images were then calculated for the thickness of the inferior, superior, nasal, and temporal quadrants retina and the global (average) thickness.

The VRQoL was assessed using the modified version of VFQ-25 in Malay language that was validated by Azreen [12]. This modified version was adjusted according to the Malay social demographic and local culture. Numeric values of items were converted to a score from 0 to 100. A score of 100 indicates better VRQoL, and 0 indicates the worst VRQoL. The interview session was done by the primary investigator.

PRP was performed using laser machine Visulas 532S (Carl Zeiss Meditec, Inc., Dublin, CA, USA) by one identified ophthalmologist. The laser setting was set with spot size of 200 - 300 µm and duration of 100 - 150 ms at a power level ranging from 200 - 400 mw to achieve a mild to moderate blanch on the retina. The laser procedure was done in three to four sessions within three weeks until a completion of minimum number of lasers shot of 3000 – 5000.

Three months after completion of PRP, the patients were reviewed again for re-assessment of VRQoL and measurement of RNFL thickness. The VRQoL questionnaire and RNFL thickness measurement were re-evaluated using the same tools by the same person.

Data were analysed using Statistical Package for Social Sciences (SPSS Inc.) version 20.0. All values were tested for normal distribution. The numerical data were tested using paired t-test. The correlation was tested using Pearson correlation. P-values of <0.05 was taken as significant.

3 RESULTS

A total of 44 PDR patients were enrolled into the study. Out of 44 patients, 26 patients (59.1%) had duration of diabetes between 11 to 20 years (Table 1). Evaluation at 3 months after completion of PRP showed 20 patients (45.5%) had complete regression of PDR while 24 patients (54.5%) experienced incomplete regression. Among the incompletely regressed group, all patients have partial resolution of macular oedema at 3 months post-PRP, and 2 patients developed neovascular glaucoma.

There was significant reduction in the mean visual acuity from pre PRP (LogMAR 0.33 SD 0.25) to at three months post PRP (LogMAR 0.54 SD 0.25, p<0.001) (Table 2). Global RNFL thickness reduced significantly at three months post PRP (p<0.001). Based on quadrant, all quadrants had significant reduction in RNFL thickness at three months post PRP except nasal quadrant (Table 2).

Table 1: Demographic data of proliferative diabetic retinopathy patients

Characteristics	n (%)
Ethnic	
Malay	41 (93.2%)
Chinese	3 (6.8%)
Gender	
Male	24 (54.5%)
Female	20 (45.5%)
Duration of DM (years)	
≤ 10	15 (34.1%)
11-20	26 (59.1%)
21-30	3 (6.8%)

Abbreviation: DM: Diabetes mellitus

Table 2: Comparison of mean visual and RNFL thickness between pre- and post-panretinal photocoagulation among proliferative diabetic retinopathy patients.

Variables	Pre-Panretinal Photocoagulation Mean (SD)	Post-Panretinal Photocoagulation Mean (SD)	p-value
Visual Acuity (LogMAR)	0.33 (0.25)	0.54 (0.25)	< 0.001
Global RNFL Thickness (µm)	112.11 (38.94)	96.46 (29.54)	< 0.001
Quadrant RNFL Thickness (µm)			
Inferior quadrant	134.77 (43.27)	116.34 (37.94)	< 0.001
Superior quadrant	129.98 (57.82)	117.23 (40.33)	0.002
Nasal quadrant	80.02 (39.11)	74.59 (28.47)	0.061
Temporal quadrant	92.80 (42.32)	77.89 (35.67)	< 0.001

Paired t-test, p < 0.05 significant
Abbreviation: LogMAR: Logarithm of the Minimum Angle of Resolution; RNFL: Retinal nerve fiber layer

The composite score of VFQ-25 showed significant reduction in VRQoL at three months post PRP (p<0.001). There was significant reduction in all subscales of VFQ-25 except for 'general health and vision', 'response to vision problem', 'general health' and 'social function' (Table 3). The composite score of VFQ-25 in PDR patients showed a significant fair negative correlation with LogMAR visual acuity post PRP (r = -0.425, p=0.004) (Figure 1). There was significant negative correlation in all subscales of VFQ-25 except for 'general health', 'general vision' and 'social function' (Table 4).

4 DISCUSSION

PRP is beneficial to treat PDR among T2DM patients. However, patients may experience some permanent decreases in peripheral, colour and night vision. In this study, we found that there was significant worsening of visual acuity, reduction of global RNFL thickness and reduction of VRQoL at three months after completion of PRP.

Table 3: Comparison of mean VFQ-25 score between pre- and post- panretinal photocoagulation among proliferative diabetic retinopathy patients.

VFQ-25	Pre-Panretinal Photocoagulation Mean (SD)	Post-Panretinal Photocoagulation Mean (SD)	p-value
Composite score	71.14 (17.05)	64.97 (15.11)	< 0.001
Subscale score			
General health & vision	59.18 (16.41)	55.54 (13.27)	0.066
Difficulty with activity	73.47 (16.98)	65.19 (17.66)	< 0.001
Response to vision problem	74.94 (22.10)	72.35 (18.44)	0.240
Near vision	68.18 (12.99)	60.45 (13.11)	< 0.001
Distant vision	65.23 (17.18)	54.77 (16.07)	< 0.001
Role limitation	67.42 (24.50)	58.52 (22.34)	0.002
General well-being	67.23 (24.83)	56.75 (21.21)	< 0.001
General health	84.09 (19.51)	82.95 (19.27)	0.599
General vision	74.15 (28.33)	67.61 (22.61)	0.030
Social function	77.56 (24.50)	75.57 (22.55)	0.454

Paired t-test, p < 0.05 significant
Abbreviation: VFQ-25: Visual Function Questionnaire-25

Table 4: Correlation between VFQ-25 and visual acuity post-panretinal photocoagulation among proliferative diabetic retinopathy patients.

VFQ-25	Correlation Coefficient (r)	p-value
Composite score	-0.425	0.004
Subscale score		
General health & vision	-0.366	0.014
Difficulty with activity	-0.417	0.005
Response to vision problem	-0.303	0.045
Near vision	-0.427	0.004
Distant vision	-0.513	<0.001
Role limitation	-0.455	0.002
General well-being	-0.425	0.004
General health	-0.295	0.052
General vision	-0.236	0.123
Social function	-0.106	0.493

Pearson correlation, p < 0.05 significant
Abbreviation: VFQ-25: Visual Function Questionnaire-25

The cause of reduction of mean visual acuity post-PRP in our study is related to 54.5% of our patients failed to achieve complete regression of PDR. Among the incompletely regressed group, all patients have partial resolution of macular oedema at 3 months post-PRP which contribute to the reduction of visual acuity. The main cause of worsening of visual acuity post PRP is macular oedema [13,14]. Macular oedema after PRP is due to retinal inflammation and increased vascular permeability that is triggered by laser therapy [14]. It usually resolves over several weeks post-procedure.

Our finding in terms of reduction of visual acuity post PRP is comparable with study done by Kaiser et al [8] and McDonald and Schatz [15]. However, Lorusso et al [16] demonstrated that there was improvement of vision and no changes of macular perfusion at six months post PRP. Dogru et al [17] found that PRP for PDR provides good visual outcome after ten years or longer. Certain vision related problems are encountered

by PDR patients after undergoing PRP. There are other after-effects of PRP such as poor night vision, deterioration of visual fields, reduced contrast sensitivity, ocular surface disease, and impaired colour vision which can also affect visual acuity [18,19].

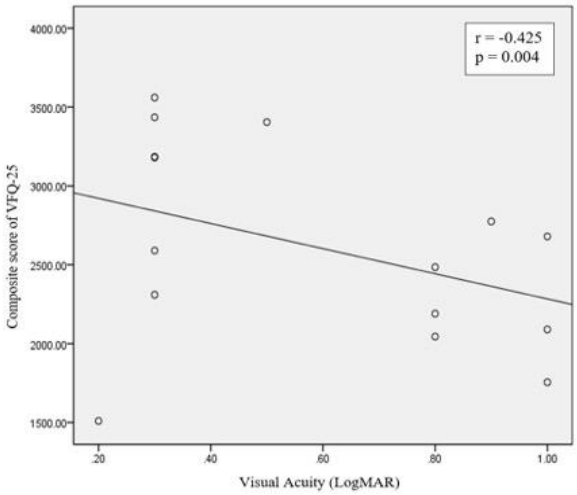

Figure 1: Correlation between composite score of Visual Function Questionnaire-25 (VFQ-25) and LogMAR visual acuity post- panretinal photocoagulation among proliferative diabetic retinopathy patients.

We found that peripapillary RNFL thickness reduced significantly at three months after completion of PRP. PRP causes direct laser damage to the axons causing axonal injury. This axonal injury may cause disruption of the mid-axonal flow which will cause retinal oedema and RNFL thickening. Axonal damage will subsequently cause cell death and lead to thinning of the RNFL [20]. DM itself can cause neurodegenerative changes in the retina and retinal thinning [21,22]. Hyperglycaemia lead to increase vulnerability to tissue viability. This in turn makes the RNFL vulnerable to external insults, such as laser [23].

Other studies also found reduction of RNFL thickness post-laser [23,24]. Yazdani et al [24] found that the thickness initially increased at one month, and subsequently reduced at six months after PRP. Kim and Cho [23] reported a significant reduction of RNFL thickness at six months. The difference in the time of thinning may be contributed by the intensity of laser burns given to the retina. A bigger spot size cause the burns to enlarge over a shorter time and cause early RNFL thinning [20]. Laser therapy lead to further thinning of RNFL thickness in diabetic eyes that already has retinal neurodegenerative changes and retinal thinning [25].

In this study, we found that the VRQoL based on VFQ-25 score was significantly reduced at three months post PRP. Contrary, Sharma et al [26] found that laser PRP significantly improve health related QoL. Russell et al [27] also found that the QoL post PRP in their patients was improved. However, they evaluated the QoL up to ten years post-laser. The discrepancy in the results could be due to the short duration of post laser therapy in our study. Diabetic patients themselves already have some reduction in QoL even before they developed DR. The development of DR in the setting of this pre-existing poor VRQoL may not add a significant effect to the patient's health in general. That might explain the reason why there was no improvement of VRQoL post PRP. In DR, VRQoL is not affected by visual acuity alone. Factors like patients' insight about their illness, control of diabetes, complications of diabetes, having to comply with the diabetic medication for years, and associated comorbidities such as hypertension, heart disease or diabetic foot ulcer may affect the patients' QoL as a whole [28-30].

Correlation between VFQ-25 scores and visual acuity in this study showed significant fair inverse relationship. When logMAR visual acuity decreased (better visual acuity), diabetic patient with PDR has better VRQoL with increased of VFQ-25 score. Vision related problems can be due to other concurrent factors such as the progression of DM itself. Diabetic complications such as nephropathy or neuropathy may also contribute to the worsening of VRQoL.

There are some limitations in this study that could be overcome in the future. Our study was carried out in a short term, which we think is the cause of discrepancy in the result of the RNFL thickness and VRQoL compared with other studies. For future studies, it is recommended for longer follow-up post-laser treatment and involve a bigger number of subjects.

5 CONCLUSION

PRP was associated with reduction of RNFL thickness and VFQ-25 composite score in T2DM patients with PDR at three months post procedure. Longer duration of follow-up is recommended to look for the long-term effect of VRQoL from the laser therapy.

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