Original Article

Measurement of the Cut Off Score of Visual Function Questionnaire on Vision Related Quality of Life to Predict Severity of Diabetic Retinopathy

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ABSTRACT

Background: *Diabetic retinopathy has a negative impact on quality of life. In order to investigate the effects of visual impairment in self-perception of quality of life, vision related questionnaires such as the National Institute Visual Function Questionnaire (NEI-VFQ-25) has been developed. The aim of this study is to predict severity of diabetic retinopathy using NEI-VFQ-25 Version 2000 by measuring the cut off score of visual function questionnaire on vision related quality of life*

Methods: *Cross Sectional study by examining 49 diabetic retinopathy patients who meet the inclusion criteria. All patients requested to answer the questionnaire. All question have a score and all question scores then categorized into a number of subscales that can be averaged to yield the subscale scores (lowest to highest range 0-100). Higher score on the VFQ–25 indicates better visual function and health related quality of life. Average scoring then being analyzed by ROC curve in order to gain the cut off score value between retinopathy and sight threatening diabetic retinopathy.*

Results: *The cut off score value between retinopathy and sight threatening diabetic retinopathy is 90.90. The VFQ-25 classification score is in the range of <90.90 consider threatening diabetic retinopathy and ≥90.90 consider retinopathy.*

Conclusion: *VFQ-25 is one of the instruments to confirm that diabetic retinopathy significantly impair quality of life. The cut off score value between retinopathy and sight threatening diabetic retinopathy is 90.90.*

Keywords: *Diabetic retinopathy, NEI-VFQ-25*

Diabetes mellitus is an important public health problem worldwide. WHO has estimated that there were 171 million people worldwide with diabetes mellitus in 2000 and predicted that 366 million people will have diabetes mellitus by 2030. [1] The Incidence of diabetes in the Asian population also seems to be on the rise.[2] The rise in prevalence is more in developing countries, of 170 % compared to 42 % in developed countries to the year 2025.[3-5] In Indonesia, the number of adults with diabetes is expected to rise from 6.9 million in 2010 to 12 million in the year 2030.[2]

Common micro vascular complication of diabetes is diabetic retinopathy. Diabetic retinopathy is leading cause of visual impairment. WHO estimated that diabetic retinopathy is responsible for 4.8% of the 37 million cases of blindness throughout the world.[1] More than 75%

of patients who have had diabetes mellitus for more than 20 years will have some retinopathy. Based on DiabCare Indonesia 2008 Study, as much as 14.5% complication of diabetic mellitus was non-proliferative retinopathy and 1.8% was proliferative retinopathy.[2]

Diabetic retinopathy has a negative impact on quality of life, particularly in the advanced stages.[5] In non-proliferative stages, diabetic retinopathy is mostly asymptomatic but may cause disabling vision loss once it progresses to advanced stages.[6] Visual impairment in diabetic retinopathy patients were associated with limitations in mobility and activities of daily living.[7] The impact of vision loss have reported affect multiple areas of well being including visual performance (visual acuity, depth perception, color, contrast sensitivity and visual field), independence, mobility, leisure and self care.[3,7]

Visual acuity has been the main outcome measure used in clinical practice and research to assess function. However visual acuity may not optimally assess ability to do specific task and does not measure a patient's self-assessment of well-being, expectations and demands. In order to investigate the effects of visual impairment in self-perception of quality of life, vision related questionnaires such as the National Institute Visual Function Questionnaire (NEI-VFQ-25) has been developed.[9]

The Visual function questionnaire (VF-QoL-25) developed to elicit patient perceptions of their visual impairment and its relation to Vision related quality of life.[7] The reliability and validity of the VFQ-25 has been demonstrated in a variety of eye conditions including cataracts, age-related macular degeneration, primary open- angle glaucoma, cytomegalovirus retinitis and diabetic retinopathy. High score on VFQ-25 indicates better visual function and health related quality of life.[7] Studies about relationship between diabetic retinopathy and vision related quality of life have been done numerously in the past. Cusisk *et al* (2005) examine the relationship between clinical measures of central vision function and the near and distance subscale. Broman *et al* (2002) assess the impact VA impairment and eye disease. Klein *et al* examine association between visual acuity and diabetic retinopathy.[3]

Based on our knowledge, no reported about measurement the cut off score of visual function questionnaire on vision related quality of life to predict severity of diabetic retinopathy using National Eye Institute Vision Related Quality of Life (VRQoL)-25 Version 2000.

MATERIAL AND METHODS

The population target for this study was all diabetic retinopathy in community. The accessible population was diabetic retinopathy patients in vitreo-retinal outpatient clinic of Cicendo Eye Hospital who meets the inclusion criteria. Inclusion criteria in this study consisted of all new and old diabetic retinopathy patients with or without complication. All patients have the ability to understand Indonesia language. Exclusion criteria including patients who were not willing to complete the questionnaire, patients with presence of diseases that might affect the possibility of irrational answer (dementia, Alzheimer), and patients with presence of disease which significantly cause visual impairment (advance cataract, optic disc swelling and optic neuropathy, BRVO). Grading cataract with nuclear opacity $\geq$ 5 (NO$\geq$5) and Posterior opacity $\geq$3 (P$\geq$3)) based on LOCS criteria were excluded from this study.

Diabetic retinopathy (DR) was defined as the presence and characteristic evolution of typical retinal microvascular lesions in an individual with diabetes. DR divided into non-proliferative DR (NPDR) and proliferative DR (PDR). Typical early NPDR lesions including micro aneurysms dot, blot or flame hemorrhage. In more advance NPDR; lesions including hard exudate, cotton wool spots or soft exudates, intraretinal microvascular abnormality (IRMA) and venous beading. Proliferative DR (PDR) is characterized by growth of abnormal new vessel and fibrous tissue in response to retinal ischemia, and subsequent development of pre-retinal or vitreous hemorrhage or fibrous proliferation. In this study severity of diabetic retinopathy was categorized based on the presence of clinical symptom related with visual function, divided into two main categories, retinopathy and sight threatening DR. Retinopathy usually

asymptomatic, consist of mild and moderate non-proliferative diabetic retinopathy. Diabetic retinopathy with potentially visual impairment or sight threatening DR consists of severe non-proliferative diabetic retinopathy, proliferative diabetic retinopathy and presence of CSME in all staging of diabetic retinopathy.

This study used questionnaire of Vision Related Quality of Life (VRQoL)-25 Version 2000 from National Eye Institute to evaluate visual function related to quality of life. These questionnaires have 25 questions that includes 1 general health item in addition to 11 visual subscale scores of general vision, ocular pain, near vision, distance vision, social function, mental health, role limitations, dependency, driving, color vision, and peripheral vision. All items have a score, items score within a subscale are averaged to yield the subscale score (lowest to highest range 0-100)[9] A high score on the VFQ–25 indicates better visual function related to quality of life.[7]

The study was cross-sectional and conducted during one month (June) in vitreo-retinal outpatient unit of Cicendo Eye Hospital, National Eye Center in Indonesia. The samples for this study were taken by consecutively. All patient underwent dilated fundus examination to define diabetic retinopathy. Severity of DR diagnosed by ophthalmologists in vitreo-retinal unit. Informed consent related with the procedure of the study was given to all candidates. The VFQ-25 version 2000 was translated in Indonesian version. Before answered the questionnaire, patient were given explanation how to fill the questionnaire. The patients were able to read and answered the questionnaire self-administrated and patient with limited visual function were interviewed to answer the questionnaire. Medical records reviews were used as additional information such as other ocular condition (presence of cataract, glaucoma, retinal detachment, BRVO), visual acuity, health related comorbidities (hypertension, chronic renal disease, cancer) and history of diabetic retinopathy therapy (Panretina photocoagulation, anti VEGF injection, pars plana vitrectomy)

To analysis the data, our study used SPSS for windows release 18.0. The score of VFQoL-25 analyzed by ROC curve to know the cut off score value between retinopathy and sight threatening diabetic retinopathy. Association cut off score of visual function questionnaire (VFQoL-25) and severity of diabetic retinopathy analyzed by fisher's Exact Test and Chi-Square test.

RESULTS

General information in ters of social-demographic characteristic about participating patient is summarized in table 1.

Table 1. Soclodemographic characteristic of diabetic retinopathy (n=49)

Characteristic	Number (%)
Median age (years)	55
Range	38-82
Sex	
Male	18 (36)
Female	31 (64)
Occupation	
Caring for family	16 (32.6)
Government employee	20 (40.8)
Employee	3 (6.1)
Labor	2 (4.1)
Retired	4 (8.2)
Private sector	4 (8.2)
Education level	
Elementary school	10 (20.4)
Junior high school	5 (10.2)
Senior high school	13 (26.5)
Academician	21 (42.9)
Complication	
DR without complication	17 (34.7)
DR with complication	
Unilateral complication	20 (40.8)
Bilateral complication	12 (24.5)
Treatment of diabetes	
Oral hypoglycemic	31 (63.2)
Insulin	7 (14.3)
Combination of insulin and oral hypoglycemic	7 (14.3)
No medication	4 (8.2)
Therapy of diabetic retinopathy	
Avastin injection	1 (2.1)
Panretinal photocoagulation	8 (16.3)
Pars plana vitrectomy	-
Combination of DR therapy	8 (16.3)
None	32 (65.3)
Comorbidity	
Hypertension	13 (26.5)
Dyslipidemia	3 (6.1)
Nephropathy	2 (4.1)
Heart disease	2 (4.1)
Others	2 (4.1)
Combination	17 (32.7)
None	11 (22.4)

From all 49 consecutive patients, the average age of the participants was 55 years old (range age 33-82 years old) with 17 male participants (34.7%) and 32 female participants (65.3%). The most common occupation of the participants were government employee (N: 20 (40.8%). The majority education levels of participants were academician (N: 21; 42.9%). About 34.7% participant had a diabetic retinopathy without complication and 65.3 percent had a diabetic retinopathy.

Complication diabetic retinopathy divided into two categories; unilateral complication (N: 20; 40.8%) and bilateral complication (N: 12; 24.5%). Complications following diabetic retinopathy include traction, vitreous hemorrhage, neovascular glaucoma, and epiretinal membrane.

To control their systemic condition of diabetic mellitus, the participans used oral hypoglycemic (N: 31; 63.2%); insulin (N: 7; 14.3%); combination of insulin and oral hypoglycemic drugs (N: 7; 14.3%); no medication (N: 4; 8.2%). The majority of patients never received any kind of therapy for diabetic retinopathy (N: 32; 65.3%). Other participant were underwent panretinal photocoagulation (N:8; 16.3%), avastin injection (N:1; 2.1%), and combination therapy consist of avastin injection, PRP and pars plana vitrectomy (N: 8; 16.3%). The systemic co-morbidities of the participans known by self-reported medical condition including hypertension (26.5%), dyslipidemia (6.1 %), nephropathy (4.1%), heart diseases (4.1%), others consist of colorectal cancer and acute myelocytic leukemia (4.1%). There are 32.7% of patients with co-morbidities in this study and 22% patients with no co-morbidity.

Table 2. Average value of severity DR related on Vision-Related Quality of Life

Category	Number	Median Score
Retinopathy		
Bilateral mild	2	91.4
Bilateral moderate NPDR	-	-
Combination of both	-	-
Sight threatening DR		
Bilateral severe NPDR	2	72.9
Bilateral PDR	20	55.8
Combination of PDR and NPDR	5	62.9
DR with CSME	20	62.2

Severity of diabetic retinopathy cases was categorized based on the presence clinical symptom related with visual function (retinopathy and sight threatening DR) and classification involving unilateral or bilateral involvement of diabetic retinopathy. There were 2 Retinopathy cases with the subscale median score of 91.4 in which most participants suffer from sight threatening DR (N: 47). The majority of the patients are classified into bilateral PDR (N: 20, median score of subscale is 55.8) and any stage of DR with CSME (N: 20 median score of subscale is 62.2). Only 2 patients categorized as bilateral severe NPDR with the subscale median score is 72.9.

ROC (Receiver Operating Characteristic) curve is used to predict the severity of diabetic retinopathy. Based on statistical calculation the cut off score value are 90.90. The VFQ-25 classification score in the range of <90.90 and >=90.90 resulting in high sensitivity and specificity (sensitivity=100.0% and specificity= 97.9%).

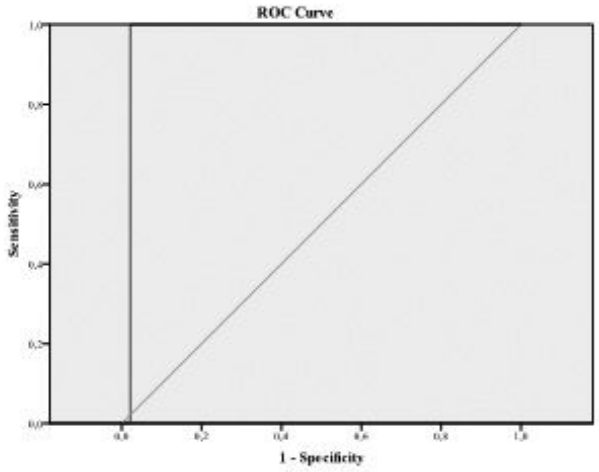

Fig 1. Cut off score analysis of visual function related quality of life (VFQoL-25) to predict severity of diabetic retinopathy

The crosstabulation shows 100% VFQoL-25 sensitivity value based on 2 patient in which the retinopathy patient predicted accurately by VFQoL-25 score of <=90.90. The sensitivity and specificity values are in accordance with the ROC curve analysis result. Positive predicted value of VFQoL-25 =66.7% (from 3 patient in which predicted as retinopathy with VFQoL-25 score >90.90; 2 patients are retinopathy). Negative predicted value of VFQoL-25=100% (from 46

Table 3. Analysis of severities of diabetic retinopathy related to the visual function related quality of life score

VFQoL-25 * Severity of Diabetic Retinopathy Crosstabulation					
			Severity of Diabetic Retinopathy		Total
			Retinopathy Sight Threatening DR		
VFQoL-25	>=90.90	Count	2	1	3
		% within severity of diabetic retinopathy	100.0%	2.1%	6.1%
	<90.90	Count	0	46	46
		% within severity of diabetic retinopathy	.0%	97.9%	93.9%
Total		Count	2	47	49
		% within severity of diabetic retinopathy	100.0%	100.0%	100.0%

patient in which predicted as sight threatening diabetic retinopathy with VFQoL-25 score <90.90; all patients are sight threatening diabetic retinopathy. Accuracy value of VFQoL-25= 98.0% (From total 49 patient, 48 patients have a predicted accurately by VFQoL-25, 2 patients are retinopathy and 46 patients are sight threatening diabetic retinopathy (P value: 0.003).

DISCUSSION

Table 1 presented the demographic profile of the patient in outpatient clinic of vitreoretinal unit in Cicendo Eye Hospital, Indonesia. The average age of the participants was 55 years old (range age 33-82 years old). American Diabetic Association reported the new cases of blindness among adults aged 20-74 years are most frequent cause by diabetic retinopathy.[10] From this study, the majority of diabetic retinopathy patients were female. Although the study about diabetic retinopathy in large participant has not yet conducted in Indonesia, the DiabCare Asia 2008 study revealed female had a greater proportion than male in diabetic patient.[2] Most of participants were government employee. This condition occurred because the study conducted in government hospital that received health government insurance. The systemic co-morbidities of the participants known by self reported medical condition including hypertension, dyslipidemia, nephropathy, heart diseases, others (cancer). Bailey and Sparrow[6] (2001) described significant levels of co-morbidity in patients with DR, including angina, myocardial infarction and renal impairment, which have an impact on the clinical management of eye disease.[5,11-13] however, the presence of co-morbidities in patients with ocular disease did not affect ocular utility values.[12,14]

From table 2, most of the participants suffered advance disease of diabetic retinopathy, only two patients suffered from asymptomatic diabetic retinopathy. The characteristic of the patients influenced by the place of the study. Cicendo eye hospital is national referral center, most of the patient referred by general ophthalmologist from district area.

Diabetic retinopathy patients were experiencing a range of physical, functional and phychosocial difficulties. Clinical measures of visual function such as visual acuity, visual field and contrast sensitivity do not provide comprehensive information on impact of vision impairment. VFQ-25 is one of the instruments to confirm that diabetic retinopathy significantly impair quality of life.[11] Two patients classified as retinopathy (mild NPDR), median score was 91.4. Most patients were classified as bilateral PDR and DR with CSME. Median score of bilateral PDR was 55.8 and median score of DR with CSME was 62.2. Two patients classified as bilateral severe NPDR. Median score was 72.9. Recent studies were suggested diabetic retinopathy impacts on patients functioning and quality of life. Gabrielian et al have reported scores 25-30 (out of 100) points lower in patients with PDR compared with those with NPDR.[10,12]

Based on our statistical calculation, the cut off score value is 90.90. The VFQ-25 classification score is in the range of <90.90 and >=90.90. Our study showed a worse self reported visual functioning in sight threatening diabetic retinopathy. In study of Varma et al about relationship between bilaterality, severity

of visual impairment and health-related quality of life, showed a distinct pattern of poorer self reported visual functioning with increasing severity of visual impairment. Participants with bilateral moderate/severe visual impairment reported the poorest visual functioning, particularly for scale including difficulty with driving, difficulty with distance and near task and vision-related dependency and mental health.[8] The result of our study showed the worse score in self reported scoring of sight threatening diabetic retinopathy are in near and distance task, mental health, role difference and dependency. Low scores for dependency and mental health demonstrate the isolating affect severe visual impairment and are reflected by a loss of independence and increase anxiety. [8]

The result of our study revealed in sight threatening disease, the scales that appeared not decrease significantly are ocular pain, visual function and color vision. The study of Varma et al showed the close result with our study. Three scales that appeared to be unrelated with visual impairment in diabetic retinopathy are color vision, ocular pain and vision-related role function. [8]

From the statistical analysis, cut off score value is 90.90. The score of >90.90 consider retinopathy and =<90.90 consider the sight threatening diabetic retinopathy. The cut off score value could be used to predict for general practitioner to know any sign visual impairment in patients with diabetic mellitus. If the lowest score has been detected, referral to ophthalmologist should be done as soon as possible.

The VFQ is an instrument that can provide clinicians and policymakers with more accurate assessment of the worth of specific healthcare intervention and can be useful adjunct to regular eye examination. Gabriellien study reported that VFQ is a superior measure of vision related quality of life (VRQOL) more accurately than visual acuity because visual acuity is only objective measure of macular function, while the eye disease can affect various aspects of vision such as glare, contrast sensitivity, colour vision and stereoscopic vision.[12,15]

There are some limitations in this study. Method of patient recruitment, small sample especially in the mild and moderate NPDR and recall bias. Consecutive method has a several limitation such as unequal distribution between retinopathy and sight threatening disease. Only 2 patients diagnose as mild diabetic retinopathy, included in asymptomatic or retinopathy classification, others included in the sight threatening diabetic retinopathy. Further research with greater sample size needs to be conducted from each category. Questionnaire in some cases were self-administered and others were interview-administered. Interview-administered would introduce selection bias because interview method can alter the patient's response to answer based on patient expectation.

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