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Factors associated with vision-related quality of life in Brazilian patients with glaucoma

Fatores associados à qualidade de vida relacionada à visão em pacientes brasileiros com glaucoma

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ABSTRACT | Purpose: To evaluate the impact of visual acuity, visual field damage, and other factors on the quality of life in Brazilian patients with glaucoma. **Methods:** This cross-sectional prospective study involved 49 patients with glaucoma enrolled based on the presence of reproducible standard automated perimetry defects in at least one eye at the time of evaluation. A detailed ophthalmologic examination was performed on each patient. All patients had reproducible standard automated perimetry and completed an NEI VFQ-25 questionnaire. The associations of the quality of life scores to the best-corrected visual acuity and the visual field loss of the better and worse eyes were investigated. **Results:** The mean quality of life score of the patients was 58.8 ± 18.7 units. The highest and lowest mean values (85.0 ± 24.2 and 37.5 ± 36.5 units) were observed in the "Social Functioning Subscale" and "Driving Subscale," respectively. Patients with advanced glaucoma (mean deviation <-12 dB) in the worse eye had significantly lower quality of life scores (p=0.007). There was a significant correlation between the quality of life scores and the visual acuity of the better and worse eyes (r^2=13%, p=0.010 and r^2=32%, p<0.001, respectively). There was also a significant correlation between the quality of life scores and standard automated perimetry mean deviation of the better and worse eyes (r^2=13%, p=0.023 and r^2=47%, p<0.001, respectively). In a multivariate model containing socioeconomic and comorbidity indices, quality of life remained significantly related to the standard automated perimetry mean deviation of the better and worse eyes (r^2=23%, p=0.29 and r^2=49%, p<0.001, respectively) as well as to the visual acuity of the better and worse eyes (r^2=18%, p=0.017 and r^2=40%, p<0.001, respectively). **Conclusion:** The standard automated perimetry mean deviation and the visual acuity of the better and worse eyes were associated with lower quality of life in Brazilian patients with glaucoma. Quality of life was mostly highly associated with the standard automated perimetry mean deviation of the worse eye.

Keywords: Glaucoma; Eye health; Quality of life; Visual field; Surveys and questionnaires/standards; Visual acuity

RESUMO | Objetivo: Avaliar o impacto da acuidade visual, danos no campo visual e outros fatores na qualidade de vida em pacientes brasileiros com glaucoma. **Métodos:** Este foi um estudo transversal prospectivo incluindo 49 pacientes com glaucoma selecionados com base na presença de defeitos por perimetria automatizada padrão reprodutíveis em pelo menos um olho no momento da avaliação. Um exame oftalmológico detalhado foi realizado em cada paciente. Todos os pacientes possuíam perimetria automatizada padrão reprodutível e preencheram um questionário NEI VFQ-25. As associações dos escores de qualidade de vida à acuidade visual melhor corrigida e à perda de campo visual dos melhores e piores olhos foram investigadas. **Resultados:** A média dos escores de qualidade de vida dos pacientes foi de 58,8 ± 18,7 unidades. Os maiores e menores valores médios (85,0 ± 24,2 e 37,5 ± 36,5 unidades) foram observados nas subescalas "Social Functioning Subscale" e "Driving Subscale", respectivamente. Pacientes com glaucoma avançado (desvio médio <-12 dB) no pior olho tiveram escores de qualidade de vida significativamente menores (p=0,007). Houve correlação significativa entre escores de qualidade de vida e a acuidade visual dos olhos melhores e piores (r^2=13%; p=0,010 e r^2=32%; p<0,001; respectivamente). Houve também uma correlação significativa entre os escores de qualidade de vida e desvios médios da perimetria automatizada padrão dos olhos melhores e piores (r^2=13%; p=0,023 e r2=47%; p<0,001; respectivamente). Em um modelo multivariado contendo dados socioeconômicos e de comorbidades, a qualidade de vida permaneceu significativamente relacionada ao desvio médio padrão da perimetria automatizada do olho melhor e pior (r^2=23%;

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p=0,29 e r^2=49%; p<0,001, respectivamente) bem como para a acuidade visual do olho melhor e pior (r^2=18%; p= 0,017 e r2=40%; p<0,001, respectivamente). **Conclusão:** O desvio padrão da perimetria automatizada padrão e a acuidade visual dos olhos melhor e pior foram associados à menor qualidade de vida em pacientes brasileiros com glaucoma. A qualidade de vida foi em grande parte altamente associada ao desvio padrão da perimetria automatizada padrão do pior olho.

Descritores: Glaucoma; Saúde ocular; Qualidade de vida; Campo visual; Inquéritos e questionários/normas; Acuidade visual

INTRODUCTION

Glaucoma is one of the most common causes of irreversible vision loss[1]. It has been estimated that by 2020, 80 million individuals worldwide will have glaucoma and that 11 million will become bilaterally blind[1]. Although blindness is the most serious consequence of glaucoma, even mild disease can significantly affect quality of life (QoL), with functional impairment associated with a higher risk of depression[2], falls[3], motor vehicle collisions[4], and reduced ability to carry out self-care activities[5]. Additionally, recent longitudinal studies have shown that glaucoma progression has a negative impact on vision-related QoL[4,6].

Among QoL evaluation tools, QoL questionnaires have been widely accepted as a valid method for specifically assessing the impact of impaired visual function on individuals[7]. The 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) is the most commonly used QoL questionnaire in patients with glaucoma[7,8] and has been shown to be highly reliable[9]. Different studies have used the NEI VFQ-25 to demonstrate an association between visual field (VF) loss and QoL[10,11]. In a cross-sectional study of 537 patients with ocular hypertension and glaucoma, van Gestel and colleagues demonstrated that binocular standard automated perimetry (SAP) and better eye mean deviation (MD) were associated with lower NEI VFQ-25 scores[12]. McKean-Cowdin and colleagues also found that more severe VF loss was associated with lower QoL; however, the location of the field defect was also important, and those with central defects had lower NEI VFQ-25 scores than those with peripheral VF loss[13]. The NEI VFQ-25 questionnaire was originally developed by Wolffsohn and Cochrane of Aston University in the UK and has been translated into a Brazilian version that was modified and culturally adapted for Brazilian patients[14,15].

Although VF loss and visual acuity (VA) loss are widely believed to be important risk factors for progressive QoL decline in patients with glaucoma, these parameters have rarely been analyzed in Brazilian populations[16,17]. The relationships between VF loss, VA, and socioeconomic factors and QoL have not yet been established in Brazilian patients with glaucoma. It is possible that the cultural and socioeconomic background of a specific population can affect the relationship between QoL and glaucoma damage.

In the present study, we assessed vision health-related QoL in Brazilian patients with glaucoma using the NEI VFQ-25 and evaluated the impact of potential influencing factors.

METHODS

This observational study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the Federal University of São Paulo. Additionally, written informed consent was obtained from all patients.

Study participants

We enrolled 49 patients with open-angle glaucoma selected from the Glaucoma Sector at Federal University of São Paulo (UNIFESP/EPM). All patients underwent a complete ophthalmologic examination that included a review of medical history, intraocular pressure measurement with Goldmann applanation tonometry (Haag-Streit, Koeniz, Switzerland), best-corrected VA, gonioscopy, slit-lamp biomicroscopy, and dilated funduscopic examination.

Glaucoma was defined as the presence of reproducible (≥2 consecutive) abnormal SAP test results on the 24-2 program of the Humphrey Visual Field Analyzer (Carl Zeiss Meditec, Inc., Dublin, CA, USA) or if progressive glaucomatous optic disc changes were noted on stereo photographs, regardless of the SAP results[18]. The glaucoma damage in the VF or in the stereo photographs had to be corresponding and compatible with glaucomatous disease. We defined abnormal SAP results as a pattern standard deviation index outside the 95% confidence limits and/or glaucoma hemifield test results outside the reference range. Only patients with open angles on gonioscopy were included. Patients were excluded if they had any ocular or systemic disease that could have affected the optic nerve or VF (simulating glaucomatous disease). All examinations were conducted within 3 months of each other.

25-Item National Eye Institute Visual Function Questionnaire

The NEI VFQ-25 was created to measure patient-reported vision-dependent function and the impact of vision problems on vision-related QoL in different ophthalmologic pathologies, including glaucoma[19-21]. The present version is the most frequently used in studies that include patients with glaucoma[12,13,22] and consists of 12 subscales, including general health, general vision, difficulties with near-vision activities, difficulties with distance-vision activities, peripheral vision, color vision, vision-specific role difficulties, vision-related dependency, mental health, social function, ocular pain, and driving difficulties. Each subscale consists of a minimum of one item and a maximum of four items. The algorithm has a scale ranging from 0 to 100, with higher scores representing better visual function.

The NEI VFQ-25 is the only widely used vision-specific QoL questionnaire that exists in a validated version in Portuguese. This instrument was introduced in the Brazilian version in 2008, with high reliability and validity, as an important tool to assess the impact of ophthalmic conditions on the vision-related QoL of patients[15]. The NEI VFQ-25 is the only instrument that can provide information that is both sensitive and specific to eye problems at the same time as providing information on the general status of the patient[21].

Demographic and socioeconomic parameters

Socioeconomic and clinical variables were included in the analysis, including gender (female, yes/no), ethnicity (black, yes/no), marital status (married, yes/no), and education level (at least high school degree, yes/no). These variables were added because they can affect patients" perceptions about QoL. All patients provided all demographic and socioeconomic information. For associated morbidities, the presence or history of several diseases and conditions were investigated, including arthritis, high blood pressure, diabetes mellitus, heart disease, stroke, depression, cancers, and asthma. A simple summation score was used to generate the comorbidity index[23]. The number of topical medications in use was noted for all patients. VA was also included using the Early Treatment Diabetic Retinopathy Study, and logMAR calculations were included in the analysis.

Statistical analysis

Descriptive statistics included the mean and standard deviation for normally distributed variables, whereas non-normally distributed data were presented as the median and interquartile range. Skewness/kurtosis tests and histograms were used to check normality.

Linear regression was performed to assess for possible associations between VF/VA and QoL. A multivariate linear regression model was also created to evaluate the effect of potentially confounding socioeconomic factors on the associations between VF/VA and QoL.

All statistical analyses were performed with the commercially available software Stata (version 13; StataCorp LP, College Station, TX, USA). The α level (type I error) was set at 0.05.

The excel file data used to support the findings of this study are included within the supplementary information file.

RESULTS

The study included 49 patients, and table 1 shows the clinical and demographic characteristics of the sample. The mean age of the patients with glaucoma was 63.8 $\pm$ 15.6 years, 69.39% were female, and 63.3% were married. The mean SAP MD of the better and worse eyes of the patients with glaucoma were -8.0 $\pm$ 6.9 dB and -18.0 $\pm$ 8.1 dB, respectively. The mean VA of the better and worse eyes of the patients with glaucoma were 0.5 $\pm$ 0.5 logMAR and 1.5 $\pm$ 0.8 logMAR, respectively. The

Table 1. Demographic and clinical findings of patients with glaucoma

	Patients with glaucoma (N=49)
Age ± SD (years)	63.79 ± 15.59
Gender (%)	
Female	34 (69.39%)
Male	15 (30.61%)
Ethnicity (%)	
Black	5 (10.20%)
Other	44 (89.80%)
VA of better eye ± SD (logMAR)	0.51 ± 0.52
VA of worse eye ± SD (logMAR)	1.48 ± 0.94
SAP MD of better eye ± SD (dB)	-8.01 ± 6.91
SAP MD of worse eye ± SD (dB)	-17.99 ± 8.10
Topical medications (yes, %)	32 (65.30%)
Pseudophakic eyes (yes, %)	20 (40.81%)
Comorbidity index ± SD	0.57 ± 0.87
Marital status (married, yes, %)	31 (63.27%)
Level of education (%)	
> high school	18 (36.73%)
< high school	31 (63.27%)

SD= standard deviation; dB= decibels.

mean numbers of comorbidities and medications were 0.6 ± 0.9 and 0.30 ± 0.31, respectively.

The mean QoL score of the glaucoma patients was 58.8 ± 18.7 units (Figure 1), and the highest and lowest mean values (85.0 ± 24.2 and 37.5 ± 36.5 units) were observed in the "Social Functioning Subscale" and "Driving Subscale," respectively (Table 2). Patients with advanced glaucoma (MD<-12 dB) in the worse eye had significantly lower QoL scores (p=0.007; ANOVA test) advanced glaucoma in the worse eye had significantly lower QoL compared to mild and moderate glaucoma patients.

Significant associations were found between the QoL scores and VA of the better and worse eyes (r^2=13%, p=0.010 and r^2=32%, p<0.001, respectively) (Figures 2 and 3, respectively). There were also significant correlations between the QoL scores and SAP MD of the better and worse eyes (r^2=13%, p=0.023 and r^2=47%, p<0.001, respectively) (Figures 4 and 5, respectively). In a multivariate model containing the socioeconomic and comorbidity indices, QoL remained significantly related to SAP MD of the better and worse eyes (r^2=23%, p=0.290 and r^2=49%, p<0.001, respectively). This model also showed that QoL remained significantly related to the VA of the better and worse eyes (r^2=18%,

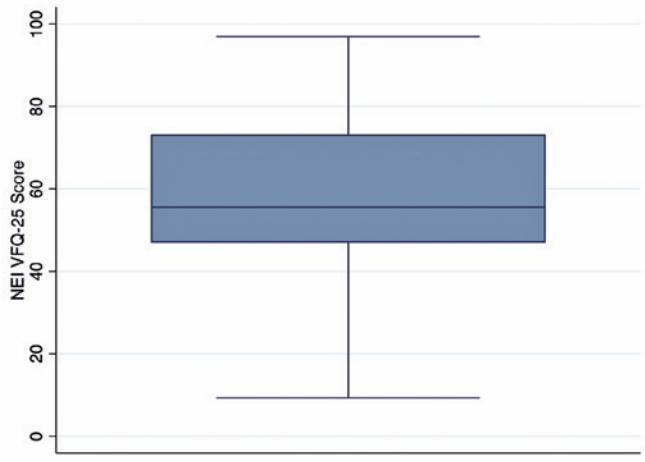

Figure 1. Boxplot depicting the distribution of the NEI VFQ-25 scores in the glaucoma group. Box: median and interquartile range (IQR). The whiskers show the maximum and minimum 1.5 IQR.

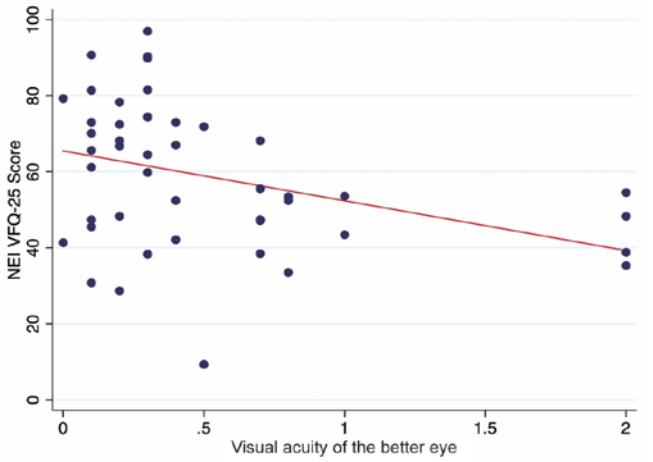

Figure 2. Scatterplot depicting the negative association between the NEI VFQ-25 scores and visual acuity of the better eye.

Table 2. NEI VFQ-25 scores and subscale results

Parameters (mean ± standard deviation)	Patients with glaucoma (N=49)
Total NEI VFQ-25 score	58.76 ± 18.70
General health	39.29 ± 22.82
General vision	61.63 ± 15.72
Ocular pain	55.61 ± 28.31
Near activities	53.47 ± 25.26
Distant activities	59.25 ± 24.98
Vision specific	
Social function	84.95 ± 24.20
Mental health	50.26 ± 24.04
Role difficulties	49.54 ± 35.24
Dependency	59.86 ± 30.74
Driving	37.50 ± 36.54
Color vision	74.49 ± 26.27
Peripheral vision	62.76 ± 30.24

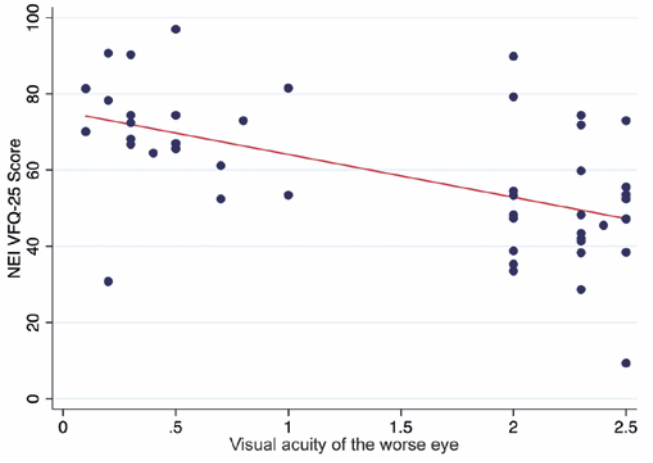

Figure 3. Scatterplot depicting the negative association between the NEI VFQ-25 scores and visual acuity of the worse eye.

p=0.017 and r^2=40%, p<0.001, respectively). No significant association was found between QoL and any of the investigated diseases and conditions (diabetes mellitus, arthritis, high blood pressure, heart disease, stroke, depression, asthma, and cancers), the number or type of topical medications in use, or with age (p>0.05 for all analyses).

DISCUSSION

In the present study, we demonstrated that the VA and SAP MD of the worse eye are significantly associated with lower NEI VFQ 25 scores. Additionally, those with advanced glaucoma had lower QoL scores than those with mild or moderate glaucoma. To the best of our knowledge, to date, only few studies have reported on the associations of VA and SAP MD with QoL in Brazilian patients with glaucoma.

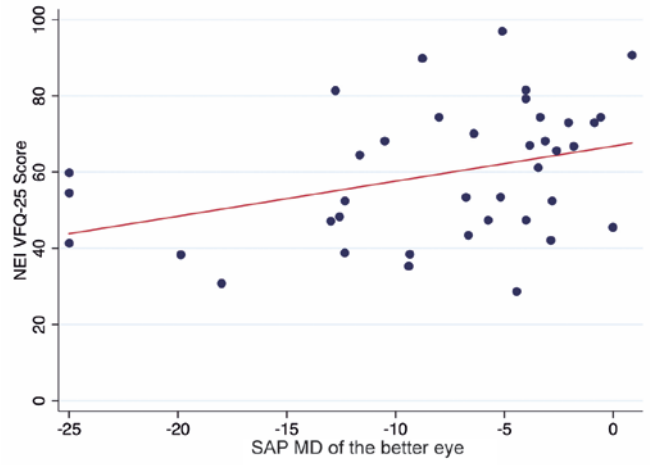

Figure 4. Scatterplot depicting the association between the NEI VFQ-25 scores and the SAP MD of the better eye.

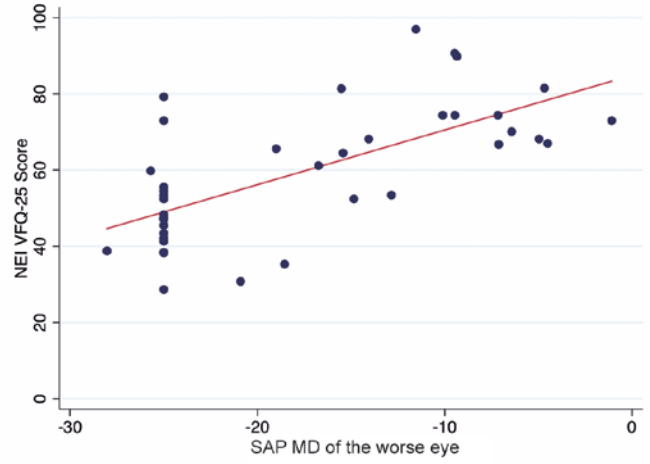

Figure 5. Scatterplot depicting the association between the NEI VFQ-25 scores and the SAP MD of the worse eye.

The significant effects of SAP MD and VA of the better eye on the QoL of patients with glaucoma have already been discussed in different populations. Van Gestel et al.[12] found in a multiple regression analysis that the coefficients of MD in the better eye were higher than those of MD in the worse eye, which indicates that VF loss in the better eye has a larger impact on QoL than VF loss in the worse eye. Additionally, the authors found that defects in the inferior hemifield require closer monitoring because they affect QoL more strongly than defects in the superior hemifield[12,24]. Although our study showed that QoL is associated with SAP MD of both the better and worse eyes, the strongest association found was between QoL and SAP MD of the worse eye. This finding is in agreement with the results of a Korean study that evaluated the QoL in 907 patients with glaucoma using the NEI VFQ-25 questionnaire and showed a significant association between QoL and worse SAP MD and VA[25]. It is possible that the functional parameters measured by VF in the worse eye are better predictors for a decline in QoL in patients with peripheral vision impairment such as glaucoma.

Progressive binocular SAP damage has also been associated with lower NEI VFQ-25 scores in longitudinal studies[6,24-27]. Gracitelli et al.[6] conducted a longitudinal study comparing retinal nerve fiber layer loss and worsening of QoL in 260 eyes of 130 patients. In their multivariate model, each 1 μm/year loss in binocular retinal nerve fiber layer (RNFL) thickness was associated with a decrease of 1.3 units per year in the NEI VFQ-25 score, which implied that a loss of 8 μm of binocular RNFL was associated with a 10-point loss in the NEI VFQ-25 score[6]. The change in binocular RNFL thickness corresponded to the change observed when using the thickest measurements between both eyes of the same patient over time; therefore, a substantial loss of RNFL had to occur in the better eye or in both eyes to produce meaningful changes in QoL. The author defends the possibility that SAP may not fully capture the changes in vision that are relevant to QoL, such as motion perception, especially when these changes occur in the macular area. In the present study, VF showed a significant association with QoL; however, it was weakly and moderately associated with the better and worse eyes

(r^2=13%, p=0.023 and r^2=47%, p<0.001), respectively. These results are in agreement with those of a previously cited longitudinal study [26,27] showing that although VF damage is related to QoL, other factors can influence this relationship. It is important to note that some of these previously cited longitudinal studies[26,27] utilized binocular RNFL or binocular VF instead of monocular VF to assess the association with QoL. In our study, we used monocular VF as a parameter. It is possible to predict binocular VF sensitivity from monocular VF test results with good accuracy for most patients with glaucoma. Further, different studies in the literature have already used different methods to predict binocular VF, such as unilateral VF or binocular summation VF, and good correlations have been found between these parameters[28].

Another interesting point is that some locations of VF damage are more strongly correlated with QoL decline than others. One longitudinal study by Abe et al.[24], which included 236 patients with glaucoma, found a significant relationship between the location of VF loss and the decline in QoL as assessed by the NEI VFQ-25. Their results showed that a progressive decline in sensitivity in the central inferior area of the VF had the strongest association with decline in QoL of patients with glaucoma when measured with the NEI VFQ-25. Loss of vision in the inferior area has a great effect on daily activities such as reading and walking down stairs or streets. The authors showed that each 1 dB/year change in binocular mean sensitivity of the central inferior area is associated with a decline of 2.6 units/year in the NEI VFQ-25 score. Our study did not address this issue, and further studies are warranted to examine whether the location of VF loss influences QoL in Brazilian patients with glaucoma.

Patients with glaucoma in the present study had difficulty driving. These results are in agreement with those of Freeman and colleagues[29], who conducted a prospective study with a 2-year follow-up involving 2520 older adults, and found that older drivers with worse visual function were more likely to modify their driving by reducing mileage and avoiding high-risk driving situations. Worse VA, contrast sensitivity, and central and lower peripheral VFs were individually associated with increased chance of reduced mileage. Further, worse contrast sensitivity and central and lower peripheral VFs were individually associated with greater odds of cessation of night-time driving, whereas worse VA was associated with increased odds of cessation of driving in unfamiliar areas. Wood et al.[30] corroborated these findings, showing that the number of collisions during simulated driving in patients with advanced glaucoma was significantly associated with decreased inferior VF mean sensitivity, in addition to older age and worse VA. Currently, driving is recognized to be a visually intensive task and is the primary mode of transportation worldwide[31]. For this reason, the ability to drive may be intimately associated with QoL, as previously reported[32].

In this study, we did not find any association between QoL and the presence of comorbidities. However, the relationships between specific chronic diseases and QoL in patients with glaucoma remain unclear. In a recent longitudinal study, Diniz-Filho et al.[33] showed that depression is associated with VF deterioration. The rates of VF change as assessed by SAP were significantly associated with depressive symptoms in patients with glaucoma who were followed up over time. Patients with rapidly progressing disease showed an increase in the incidence of depressive symptoms, as assessed by changes in the test results of a previously validated depression scale. It is possible that patients with relatively slower VF progression may have more time to adapt to their limited functional status by developing compensatory strategies that could decrease the impact of the disease, and therefore, would be at lower risk of developing or reporting depressive symptoms.

Three previous studies have evaluated QoL in Brazil. In the first study performed in a Brazilian population, Guedes et al.[34] performed a cross-sectional study on 225 patients, comparing the QoL in three patient groups who underwent different types of treatment: medical treatment, surgical treatment, and both treatments. They showed that early-stage patients with glaucoma who underwent surgery to treat their glaucoma tended to have a lower QoL score in the NEI VFQ-25, mainly because of the psychological burden. In those with moderate or advanced glaucoma, the QoL scores did not differ between the surgical and medical therapy groups. In another cross-sectional study, Guedes et al.[16] compared the QoL of patients with glaucoma who underwent medical therapy with different prostaglandins; the results showed that bimatoprost users had a lower QoL than latanoprost and travoprost users, and this difference could not be explained by the presence of any comorbidities. Bimatoprost is believed to yield a slightly better result in terms of intraocular pressure reduction and cost-effectiveness ratio; however, it is known to have the highest incidence of local side effects among all the prostaglandins and has been demonstrated to have a poor persistency profile. The side effects of bimatoprost

could lead to a worse self-perception of disease severity[16]. A recent study performed by Portela et al. used keratograph analysis and NEI VFQ-25 scores to evaluate ocular surface disease and QoL, respectively, in Brazilian patients with glaucoma. They showed that patients with glaucoma (who were using topical medications) had significantly worse ocular surfaces (as measured by keratograph analysis) and QoL (as measured by NEI VFQ-25 scores) than the control group[35].

In our study, the topical medications used and the number of topical medications used did not affect QoL. Because of our limited sample size, we stratified our analysis based on the class of topical medication. Further studies are necessary to clarify the influence of the class of topical medication on QoL in patients with glaucoma.

Our study has some limitations. First, we had a relatively small sample; however, although the present study had only 49 patients, it is the first study attempting to find an association between QoL and clinical and socioeconomic factors in a specific Brazilian population. Second, the main measure of this study was the NEI VFQ-25 questionnaire, which is a self-reported questionnaire that may be influenced by self-perception and may vary according to individual perception. Third, although we found a significant association of QoL with the VA and SAP MD of the better and worse eyes, the correlations were weak, which could be explained by the fact that there are likely other factors or confounding factors that can influence an individual's self-perceived QoL. Therefore, an individual's response to a specific vision-related QoL questionnaire item may be influenced by the individual's particular perspectives and concerns. Fourth, although patients with other ocular diseases such as cataract were excluded, it is possible that some patients could have had early nuclear sclerosis, which can also affect VA and QoL. Previous studies have already shown the negative influence of cataract on QoL[36,37], and further longitudinal studies are warranted to elucidate the influence of cataract on stable glaucoma. Lastly, because of our limited sample size, we could not run more sophisticated analyses such as Rasch analysis. Rasch scores can be used to express where each respondent falls on a linear scale, representing the level of impairment as measured by the NEI VFQ-25 and can also be used in subsequent parametric statistical analyses[32,33]. However, although Rasch analysis is an important statistical tool in this type of study, the method has some limitations in that it can be extremely restrictive because an assumption of the model is that all items have equal discrimination.

In conclusion, our results in this study of Brazilian patients with glaucoma were in agreement with those of similar studies conducted in other countries. SAP MD and VA were found to be associated with lower QoL scores, and SAP MD of the worse eye was demonstrated to be the most strongly associated factor with QoL. QoL was not correlated with the presence of comorbidities. Although our small sample and the use of a self-reported QoL questionnaire may have resulted in stronger correlations, our findings lead us to a new perspective in Brazil to help patients at a high risk of disability from glaucoma.

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