Implementation of risk stratification for the care of glaucoma patients during the resumption of in-person care during the COVID-19

Cristina Nery Carbajo, Glaucia Luciano da Veiga, Rodrigo Toledo Mota, Fernando Luiz Affonso Fonseca, Vagner Loduca Lima

Abstract

Introduction: The COVID-19 pandemic sparked a serious health crisis in which non-essential medical services were suspended, with the management of serious diseases not related to the pandemic, including glaucoma, becoming secondary in importance. With the flexibilization of social isolation measures, resuming outpatient care was necessary, respecting the health equity provided by the Brazilian Unified Health System.

Objective: To describe a risk classification of glaucoma progression based on clinical ophthalmology criteria during the COVID-19 pandemic.

Methods: Observational study of an administrative nature. A review was carried out of the medical records of patients who had scheduled appointments between March and September of 2020 in the glaucoma sector of the FMABC University Center’s Department of Ophthalmology. A total of 489 medical records (881 eyes) were reviewed, and patients were divided into 4 groups according to the risk of glaucoma progression. Eyes were evaluated for visual acuity (VA), optic disc cup, pachymetry, intraocular pressure (IOP), mean number of eyes drop medications used, and global visual field indexes.

Results: Groups were homogeneous in terms of age (mean 67.04 ± 11.72 years) and sex (55.5% women and 44.5% men). Primary open-angle glaucoma was the most prevalent etiology, present in 45.2% of patients, followed by primary angle-closure glaucoma in 15.7%. The groups were compared with each other, and a statistical difference (p<0.005) was found in 04 of the 08 aspects analyzed: VA, optic disc cup, IOP and mean number of eyes drop medications used.

Conclusion: The risk classification for progression proposed in this study was easily applied and aided managers in prioritizing the most serious care during the COVID-19 pandemic.

Keywords: glaucoma, blindness, COVID-19, pandemic.

INTRODUCTION

Currently, glaucoma is recognized as a significant public health concern, being the leading cause of irreversible blindness worldwide. Irreversible visual impairment negatively impacts both the physical and mental well-being of patients, increasing their vulnerability to accidents, social withdrawal, and depression. It is estimated that in 2020, there were 76 million people affected by glaucoma globally, and with the aging population, this number is projected to reach approximately 111.8 million by 2040. In Brazil alone, the Brazilian Council of Ophthalmology estimates that there are 985,000 glaucoma patients aged 40 and above.

Glaucoma is characterized as a progressive optic neuropathy where the evaluation of the optic disc is crucial. Changes in the neuroretinal rim due to the loss of ganglion cell axons are early indicators of the disease before peripheral vision defects occur. Qualitative assessment of the optic nerve can be performed through direct observation of the fundus using techniques such as direct ophthalmoscopy and fundoscopy. These observations can be documented using photographic filters like red-free retinography. Additionally, digital imaging techniques like Gdx, HRT, and Optical Coherence Tomography (OCT) can be employed to evaluate the optic nerve and nerve fiber layer. Progressive thinning of the neuroretinal rim and loss of the nerve fiber layer are accompanied by functional losses, ultimately impacting the patients’ quality of life. Functional losses can be quantified through standard automated perimetry (SAP) or visual field (VF) assessments. Notably, VF assessments are better suited for detecting late-stage functional loss when ganglion cell loss exceeds 50%. However, their reliability relies on patient comprehension and cooperation. Therefore, a comprehensive assessment of glaucomatous lesions necessitates the integration of quantitative assessments of both functional and structural losses.

A simple and reliable model for stratifying the severity of functional loss in glaucoma, based on both functional and structural alterations, would be valuable for both clinical research and routine outpatient care. Several classification models for glaucoma patients have been proposed; however, there is no consensus on which model is most suitable. Upon reviewing the literature, it becomes evident that each of these systems has numerous limitations, often lacking clarity in individual patient classification.

The year 2020 was marked by a severe global health crisis due to the emergence of the novel coronavirus (SARS-CoV-2) in December 2019 in China. The rapid increase in cases prompted the World Health Organization (WHO) to declare a pandemic on March 11, 2020. Although SARS-CoV-2 may not be as lethal as other viruses in the same family, its high transmissibility has led to a significantly higher number of deaths. As a result, authorities have implemented stringent social distancing measures, including lockdowns, closure of non-essential services, and suspension of elective surgeries and outpatient care.

These social isolation measures resulted in the complete cessation of medical services at the glaucoma outpatient clinic of the FMABC University Center on March 18, 2020. From March 2019 to November 2019, this clinic provided care to a total of 3,522 patients, all through the Unified Health System (SUS). As social isolation measures were gradually eased, there arose a need to stratify the risk of glaucoma progression for patients whose appointments had been canceled. This was necessary to reconstruct and organize the resumption of care, prioritizing patients with more severe conditions and a higher risk of irreversible vision loss. This approach aligns with the ethical principle of equity provided by SUS.

The objective of this study was to describe a classification system adapted from the Moorfields Eye Hospital (MEH) algorithm to the specific context of the glaucoma department at Centro Universitário FMABC. This classification aimed to assess the risk of disease progression and prioritize care for glaucoma patients during the COVID-19 pandemic.
METHODS

This observational and administrative study is based on the review of medical records of patients from the glaucoma outpatient clinic of the Ophthalmology Department of the Centro Universitário FMABC (Santo André, Brazil). Inclusion and exclusion criteria: All patients with scheduled appointments between March 18, 2020 and September 4, 2020 were included. No exclusion criteria were applied in this study.

To perform risk stratification, a team of volunteer physicians was organized, consisting of five ophthalmology residents and a glaucoma preceptor. Each team member individually reviewed the medical records of the patients, gathering clinical data and relevant diagnostic tests.

In order to develop a user-friendly risk classification system, we adapted the algorithm proposed by the Moorfields Eye Hospital (MEH) to suit the specific context of the glaucoma outpatient clinic. The following data were evaluated: best-corrected visual acuity (VA), intraocular pressure (IOP) (average of the last three visits), optic disc cupping, pachymetry, glaucoma etiology, optical coherence tomography (OCT) of the nerve fiber layer, and analysis of visual field (VF) loss progression. Additionally, factors such as indications for anti-glaucoma surgery, postoperative conditions, laser procedures (e.g., iridotomy), use of hypotensive eye drops, previous glaucoma surgeries, time since the last medical consultation, and the most recent management plan provided by the glaucoma sector were considered.

Based on the risk of progression to irreversible vision loss, patients were categorized into different color-coded groups (table 1). The groups are as follows:

### Table 1: Epidemiological and ophthalmological profile of the studied population

| Green          | Yellow                          | Orange                                      | Red
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>New cases</td>
<td>After switching eye drops</td>
<td>With scheduled surgery and preoperative exams</td>
<td>With scheduled surgery and preoperative exams</td>
</tr>
<tr>
<td>Other</td>
<td>Visual field progression</td>
<td>Post-operative &gt; 2 months</td>
<td>Post-operative &lt; 2 months</td>
</tr>
<tr>
<td></td>
<td>Follow-up in 4 to 8 weeks</td>
<td>Post-iridotomy</td>
<td>Follow-up in &lt; 4 weeks</td>
</tr>
</tbody>
</table>

Red: This group consists of patients who are at a high risk of progression in a short period of time. It includes individuals with indications for anti-glaucoma surgery (such as trabeculectomy, drainage device implantation, needling, and cyclophotocoagulation) who have already undergone preoperative tests. It also includes patients who are in a 2-month postoperative state and those whose medical management plan requires a follow-up within 4 weeks. These patients are considered to have poorly controlled glaucoma and a higher risk of developing irreversible nerve damage rapidly.

Orange: This group comprises patients with a moderate-to-high risk of progression in a short period of time. It includes individuals with indications for anti-glaucoma surgery who have not undergone preoperative exams. It also includes patients who are in a postoperative state between 2 and 6 months (considered late postoperative) and those who have undergone laser procedures.

Yellow: Patients in this group are at a moderate risk of progression in a short period of time. It includes individuals with indications for changing their topical hypotensive medication, as this is considered indicative of poor intraocular pressure (IOP) control. Additionally, patients with recorded progression of functional visual field (VF) loss and those with an expected follow-up in 4 to 8 weeks are classified in this group.

Green: This group consists of patients at a low risk of progression in a short period of time. It includes all patients who do not meet the criteria for the aforementioned groups and are considered to have well-controlled glaucoma. Additionally, new cases are categorized as green following the algorithm proposed by the Moorfields Eye Hospital, as these patients have not yet been evaluated by glaucoma specialists.

The data for each eye of the individuals included in this study were analyzed separately. However, a consensus was reached to classify each patient based on the eye with the most advanced disease. For example, if a patient had advanced neovascular glaucoma in one eye classified as red, while the contralateral eye did not show glaucomatous alterations and was in the green group, the patient would be included in the red group.

Patients were considered “single eye” cases only if the best-corrected visual acuity in one eye was absence of light perception (SLP). In these cases, the patient was classified one color above the initially proposed classification based on the analysis of their ophthalmological data and complementary examinations of the contralateral eye. These patients were considered to be in a more serious condition due to having only one functional eye and therefore had a higher likelihood of developing bilateral blindness.

Following the resumption of medical services, all health measures recommended by the Brazilian Ministry of Health were strictly followed. It was decided that 10 patients would be seen per day, starting with those in the red group and progressing to the orange and yellow groups. Finally, after greater flexibility in August 2020, patients in the green group were scheduled. All patients were actively screened via telephone for respiratory symptoms, fever, and malaise. They were instructed not to attend their appointments if they had any positive symptoms. Additionally, the scheduling of appointments was left to the discretion of each patient. Long-term outpatient follow-up was guaranteed, even for those who chose not to attend their appointments due to fear of COVID-19 contagion.

Data Analysis

Data were presented as absolute values and percentage, mean and standard deviation of the mean.
For the correlation analysis, the one-way ANOVA test was applied. To evaluate statistical differences, GraphPad Prism® Software version 6.0 was used. Values were considered statistically significant when p<0.05.

**RESULTS**

A total of 489 medical records were reviewed, of which 271 were women (55.5%) and 218 were men (44.5%) aged between 20 and 93 years (table 1). Of all the patients analyzed, 881 eyes were included in this study. The most prevalent etiology was primary open-angle glaucoma (POAG) present in 221 patients (45.2%), followed by primary angle-closure glaucoma (POCG) in 77 patients (15.7%) and in third, 50 patients undergoing investigation for suspected glaucoma (10.2%).

Regarding hypotensive eye drops, there are 04 classes of drugs currently available on the market: β-blockers, carbonic anhydrase inhibitors, α-agonists and prostaglandin analogues. There are 11 possible combinations in addition to monotherapy, the most frequent being the combination of prostaglandin analogue + β-blocker + carbonic anhydrase inhibitor for IOP control in 122 eyes (14%), followed by the combination of prostaglandin analogue + β-blocker in 91 eyes (10.4%). The maximal medical therapy using a combination of the 04 classes was observed in 73 eyes (8%) and 05 patients in the red group were using an oral carbonic anhydrase inhibitor (acetazolamide) concomitantly with topical therapy. The systemic use of a carbonic anhydrase inhibitor therefore indicates greater disease severity in the patient.

β-blockers were prescribed to 517 eyes (59%), consisting of the most used class by outpatients (table 2). The mean number of eyes drop medications used was 2.24 ± 0.99 for all the eyes evaluated.

All the data evaluated divided into groups are shown in table 4. Between-group comparisons showed statistical significance in 04 of the 08 analyzed components (figure 1). Of note among these was excavation of the optic nerve, which was greater in the yellow (0.76 ± 0.17), orange (0.84 ± 0.16) and red (0.79 ± 0.22) groups in relation to the green group (0.68 ± 0.18) (p=0.0001) (table 4).

Regarding VA, eyes that presented VA ≤ 0.05 (20/400) were excluded from the analysis due to being considered legally blind and VA was difficult to quantify (hand movement, counting fingers, light perception and without light perception). The difference between VA in the eyes of the orange and red groups and of the green and yellow groups was statistically significant (p=0.0006), being lower in the orange and red groups (table 3).

For the analysis of IOP, the only modifiable risk factor for glaucoma, we used the simple mean of the last three measurements contained in clinical records. From the mean IOP, a statistically relevant difference (p=0.0484) was possible to identify between the IOP of the orange group and the other groups (table 3).

The mean amount of eye drop medications used also proved to be statistically significant (p = 0.0013), and was higher in the yellow and orange groups when compared to the green and red groups. On average, eyes in the yellow and orange groups used 2.01 ± 1.21 and 2.38 ± 1.43 hypotensive eye drops, respectively, while eyes in the green group used 1.64 ± 1.19 and the red group, 1.62 ± 1.68 (table 3).

Comparison of the mean ages between the groups was not statistically significant (p = 0.3124), as well as pachymetry measurements (p = 0.0586). Both are risk factors for the development of glaucoma, but these were not associated with more severe forms of the disease. Of the 330 VF exams tabulated in this study, 222 (67.2%) were reliable and 108 (32.8%) were unreliable. In order for the VF to be considered reliable, the exam should show < 20% of fixation losses, < 33% of false positives. The global indexes of Mean Deviation (MD) and Pattern Standard Deviation (PSD) of the reliable VFs were evaluated, which showed no significant difference between groups (p = 0.5080 and p = 0.2722, respectively) (table 3).

**Table 2: Hypotensive eye drops**

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>&lt; 65 years</th>
<th>65 – 79 years</th>
<th>&gt; 79 years</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>54.97 ± 9.82</td>
<td>71.29 ± 4.03</td>
<td>83.87 ± 3.56</td>
<td>55.5%</td>
<td>44.5%</td>
<td>489</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA (mean ± SD)</td>
<td>1.0 – 0.06</td>
<td>0.61 ± 0.27</td>
<td>&lt; 0.05</td>
<td>--</td>
<td>--</td>
<td>762</td>
</tr>
<tr>
<td>IOP (mean ± SD)</td>
<td>14.3 ± 3.92</td>
<td>0.71 ± 0.19</td>
<td>SPL</td>
<td>--</td>
<td>--</td>
<td>760</td>
</tr>
<tr>
<td>Optic disc cup (mean ± SD)</td>
<td>525.53 ± 37.07</td>
<td>2.24 ± 0.99</td>
<td>Total</td>
<td>881</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Continuation - Table 2: Hypotensive eye drops

<table>
<thead>
<tr>
<th>Class / Association</th>
<th>β-blocker</th>
<th>Carbonic anhydrase inhibitor</th>
<th>α-agonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>99</td>
<td>07</td>
<td>06</td>
</tr>
<tr>
<td>Double association</td>
<td>176</td>
<td>78</td>
<td>40</td>
</tr>
<tr>
<td>Triple association</td>
<td>169</td>
<td>152</td>
<td>63</td>
</tr>
<tr>
<td>Maximal therapy</td>
<td>73</td>
<td>73</td>
<td>73</td>
</tr>
<tr>
<td>Total(n*)</td>
<td>517</td>
<td>310</td>
<td>182</td>
</tr>
</tbody>
</table>

Table 3: Group profiles

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Green</th>
<th>Yellow</th>
<th>Orange</th>
<th>Red</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>67.25 ± 10.91</td>
<td>68.15 ± 13.6</td>
<td>64.15 ± 13.22</td>
<td>66.12 ± 10.77</td>
<td>0.3124</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>Female: 196 (57)</td>
<td>51 (51)</td>
<td>16 (48)</td>
<td>8 (47)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male: 143 (43)</td>
<td>49 (49)</td>
<td>17 (52)</td>
<td>9 (53)</td>
<td></td>
</tr>
<tr>
<td>Eyes (n)</td>
<td>580</td>
<td>199</td>
<td>61</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>VA (mean ± SD)</td>
<td>0.63 ± 0.27</td>
<td>0.56 ± 0.26</td>
<td>0.43 ± 0.27</td>
<td>0.46 ± 0.25</td>
<td>0.0006</td>
</tr>
<tr>
<td>IOP (mean ± SD)</td>
<td>13.92 ± 3.40</td>
<td>14.9 ± 4.39</td>
<td>15.64 ± 5.32</td>
<td>14.33 ± 5.02</td>
<td>0.0484</td>
</tr>
<tr>
<td>optic disc cup (mean ± SD)</td>
<td>0.68 ± 0.18</td>
<td>0.76 ± 0.17</td>
<td>0.84 ± 0.16</td>
<td>0.79 ± 0.22</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pachymetry (mean ± SD)</td>
<td>524.38 ± 34.86</td>
<td>524.07 ± 41.04</td>
<td>523.81 ± 24.8</td>
<td>548.62 ± 38.78</td>
<td>0.0586</td>
</tr>
<tr>
<td>Eye drop medications used (mean ± SD)</td>
<td>1.64 ± 1.19</td>
<td>2.01 ± 1.21</td>
<td>2.38 ± 1.43</td>
<td>1.62 ± 1.68</td>
<td>0.0013</td>
</tr>
<tr>
<td>Visual field</td>
<td>MD (mean ± SD)</td>
<td>-4.27 ± 6.27</td>
<td>-5 ± 7.57</td>
<td>-10.64 ± 12.27</td>
<td>-5.95 ± 5.91</td>
</tr>
<tr>
<td>PSD (mean ± SD)</td>
<td>2.94 ± 3.18</td>
<td>2.9 ± 3.84</td>
<td>4.46 ± 4.49</td>
<td>4.75 ± 4.94</td>
<td>0.2722</td>
</tr>
</tbody>
</table>

*Assessment of VA was limited to values between 0.06 and 1.0, patients with VA ≤ 0.05 are considered legally blind and were excluded from the analysis.

Figure 1. Graph representing patient stratification, average ages of the participants and the evaluations carried out during medical consultations in the resumption of in-patient appointments during the SARS-CoV-2 pandemic. * Statistically significant variables (p < 0.05)
Several classifications for glaucoma patients have been proposed in the literature\textsuperscript{15-17}. The main systems include the Advanced Glaucoma Intervention Study (AGIS), Collaborative Initial Glaucoma Treatment Study (CIGTS), Esternan binocular scale, and Bascom Palmer GSS (Hodapp-Anderson-Parrish)\textsuperscript{18}. These systems utilize visual field (VF) data to categorize patients into mild to advanced glaucoma groups. However, our study did not find any statistically significant differences among the stratification groups when comparing the mean deviation (MD) and pattern standard deviation (PSD) values. This suggests a limitation in using VF as a sole tool for classifying glaucoma patients, as it requires patients to have a good understanding of the test for reliable results.

Bommakanti et al.\textsuperscript{17} developed an algorithm for medical screening of glaucoma patients during the COVID-19 pandemic, taking into account both the severity of glaucoma and the risk of COVID-19 transmission during ophthalmological appointments. In their study, patients classified as belonging to a high-risk group for the pandemic but with a low risk of glaucoma progression had their appointments rescheduled based on a numerical score. In our study, since all appointments were suspended and our objective was to organize the resumption of medical appointments while avoiding patient congestion, we chose not to consider patient comorbidities in our color classification\textsuperscript{19}.

The classification proposed in this study was conducted retrospectively and was not intended to stratify the severity of glaucoma or guide treatment decisions, but rather to serve as a tool for public health policy, ensuring the principles of SUS (Brazil’s Unified Health System): equity, comprehensiveness, and universality. Risk stratification based solely on clinical criteria allows estimation of which patients should be prioritized for ophthalmologist visits, ensuring optimal care for the population.

Long-term follow-up of the patients analyzed in this study is necessary to assess their progression and identify any potential shortcomings in the proposed screening process. Furthermore, long-term follow-up is crucial to confirm the ophthalmological clinical parameters that are most relevant for risk stratification of glaucoma progression.
**CONCLUSION**

The risk stratification presented in this study was derived solely from clinical and ophthalmological examination data extracted from medical records, without the need for additional tests. This approach aimed to create a classification system that is easily applicable by general ophthalmologists. Through this study, we successfully developed a risk stratification model for glaucoma patients during the resumption of in-person care amidst the COVID-19 pandemic.

The implementation of the proposed approach in the Ophthalmology Outpatient Clinic of Centro Universitário FMABC had several positive aspects, as it facilitated the provision of care for all glaucoma cases during this challenging period. By employing this risk stratification system, we were able to prioritize patients effectively and ensure the delivery of appropriate and timely care to those in need.

**Author Contributions**

All authors contributed to the manuscript.

**Conflicts of Interest**

The authors report no conflict of interest.

**REFERENCES**

17. Bommakanti NK et al. “Application of the sight outcomes research collaborative ophthalmology data repository for triaging patients with glaucoma and clinic appointments during pandemics such as COVID-19.” JAMA ophthalmology 138.9 (2020): 974-980.
Resumo

Introdução: a pandemia de COVID-19 desencadeou uma grave crise sanitária em que foram suspensos os serviços médicos não essenciais, passando a ter importância secundária a gestão de doenças graves não relacionadas com a pandemia, incluindo o glaucoma. Com a flexibilização das medidas de isolamento social, foi necessária a retomada do atendimento ambulatorial, respeitando a equidade em saúde proporcionada pelo Sistema Único de Saúde.

Objetivo: descrever uma classificação de risco de progressão do glaucoma com base em critérios oftalmológicos clínicos durante a pandemia de COVID-19.

Método: estudo observacional de natureza administrativa. Foi realizada uma revisão dos prontuários dos pacientes que tiveram consultas agendadas entre março e setembro de 2020 no setor de glaucoma do Departamento de Oftalmologia do Centro Universitário FMABC. Um total de 489 prontuários (881 olhos) foi revisado e os pacientes foram divididos em 4 grupos de acordo com o risco de progressão do glaucoma. Os olhos foram avaliados quanto à acuidade visual (AV), escavação do disco óptico, paquimetria, pressão intraocular (PIO), número médio de colírios usados e índices globais de campo visual.

Resultados: os grupos foram homogêneos quanto à idade (média 67,04 ± 11,72 anos) e sexo (55,5% mulheres e 44,5% homens). O glaucoma primário de ângulo aberto foi a etiologia mais prevalente, presente em 45,2% dos pacientes, seguido do glaucoma primário de ângulo fechado em 15,7%. Os grupos foram comparados entre si, sendo encontrada diferença estatística (p<0,005) em 04 dos 08 aspectos analisados: AV, escavação do disco óptico, PIO e número médio de colírios utilizados.

Conclusão: a classificação de risco para progressão proposta neste estudo foi de fácil aplicação e auxiliou os gestores a priorizar os cuidados mais graves durante a pandemia de COVID-19.