

Critical pathway for primary open angle glaucoma diagnosis

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Received: 2016-11-08 Accepted: 2017-02-07

Abstract

• **AIM:** To develop a critical pathway for primary open angle glaucoma (POAG) diagnosis intended to be efficient, to unify criteria, reduce resource use and minimize costs to the health system.

• **METHODS:** We performed a systematic search on PubMed, Cochrane, Embase and ClinicalTrials.org databases and classified the quality of evidence from level I through III.

• **RESULTS:** A critical pathway was designed by setting a key-decision step by step model on the basis of the best current evidence.

• **CONCLUSION:** A critical pathway, evidence-based guideline, may be a useful tool intended to reduce costs while maintaining or even improving the quality of care for diagnosing a highly prevalent pathology such as open angle glaucoma.

• **KEYWORDS:** glaucoma; diagnosis; critical pathway; guideline

DOI:10.18240/ijo.2017.06.21

Allocco AR, Ponce JA, Riera MJ, Magurno MG. Critical pathway for primary open angle glaucoma diagnosis. *Int J Ophthalmol* 2017;10(6):968-972

INTRODUCTION

Glaucoma affects more than 60 million people and represents the second leading cause of blindness worldwide. Primary open angle glaucoma (POAG) is the most frequent type of glaucoma, affecting almost 45 million people over the globe. Blindness caused by glaucoma affects 8.4 million people nowadays, and this number is estimated to rise up to 11 million people for the year 2020^[1-2].

Prompt diagnosis and treatment of ocular hypertension (OH) and glaucoma can diminish the permanent visual field loss and optic nerve head (ONH) damage observed in these patients^[2-4]. This highlights the significance of reckon on with an effective diagnosis strategy that allows to optimize resources and, mainly, gain time. Glaucoma is commonly diagnosed using

several ancillary tests and in fact there is no unique screening method that has proven to be totally effective by its own^[2]. This explains several situations of delayed diagnosis seen on these patients, which finally leads to permanent and irreversible visual loss.

Critical pathway guidelines have emerged as improving proposals for making decisions, applied for both diagnosis and treatment of specific pathologies. Particularly, critical pathways have been successfully applied for emergency pathologies in order to optimize time and resources, unifying medical criteria for making decisions^[5]. Considering the high prevalence of POAG and its irreversible consequence, we thought to be necessary to have a step by step model of taking decisions on the basis of the best current evidence.

The purpose of this paper is to develop a critical pathway for POAG diagnosis intended to be efficient, to unify criteria, reduce resource use and minimize costs to the health system.

MATERIALS AND METHODS

Critical pathway was designed by setting a key-decision step by step model on the basis of the current evidence. We performed a systematic search on PubMed, Cochrane, Embase and ClinicalTrials.org databases using the following search terms: “primary open angle glaucoma”, “critical pathway”, “ocular hypertension”, “IOP”, “glaucoma epidemiology”, “glaucoma diagnosis”, “gonioscopy”, “visual field in glaucoma”, “pachymetry”, “glaucoma progression”.

The aim of a critical pathway is to reach efficiency, to minimize treatment variability among clinicians, to shorten times and to minimize the resources and costs. Therefore, critical review and proper classification of the quality of the evidence is crucial to support this model. Thus, articles were classified according to their scientific quality from level I through III following the guidelines of the Preferred Practice Patterns of the American Academy of Ophthalmology^[3,6]. Briefly, level I included evidence obtained from at least one properly conducted, well designed, randomized and controlled clinical trial, as well as Meta-analysis including this type of studies. Level II, well-designed, controlled trials without randomization and cohort or control-case studies. Finally, level III included descriptive studies, case reports and expert consensus.

Inclusion criteria for critical pathway were patients that reach to ophthalmologic examination for the first time and also those

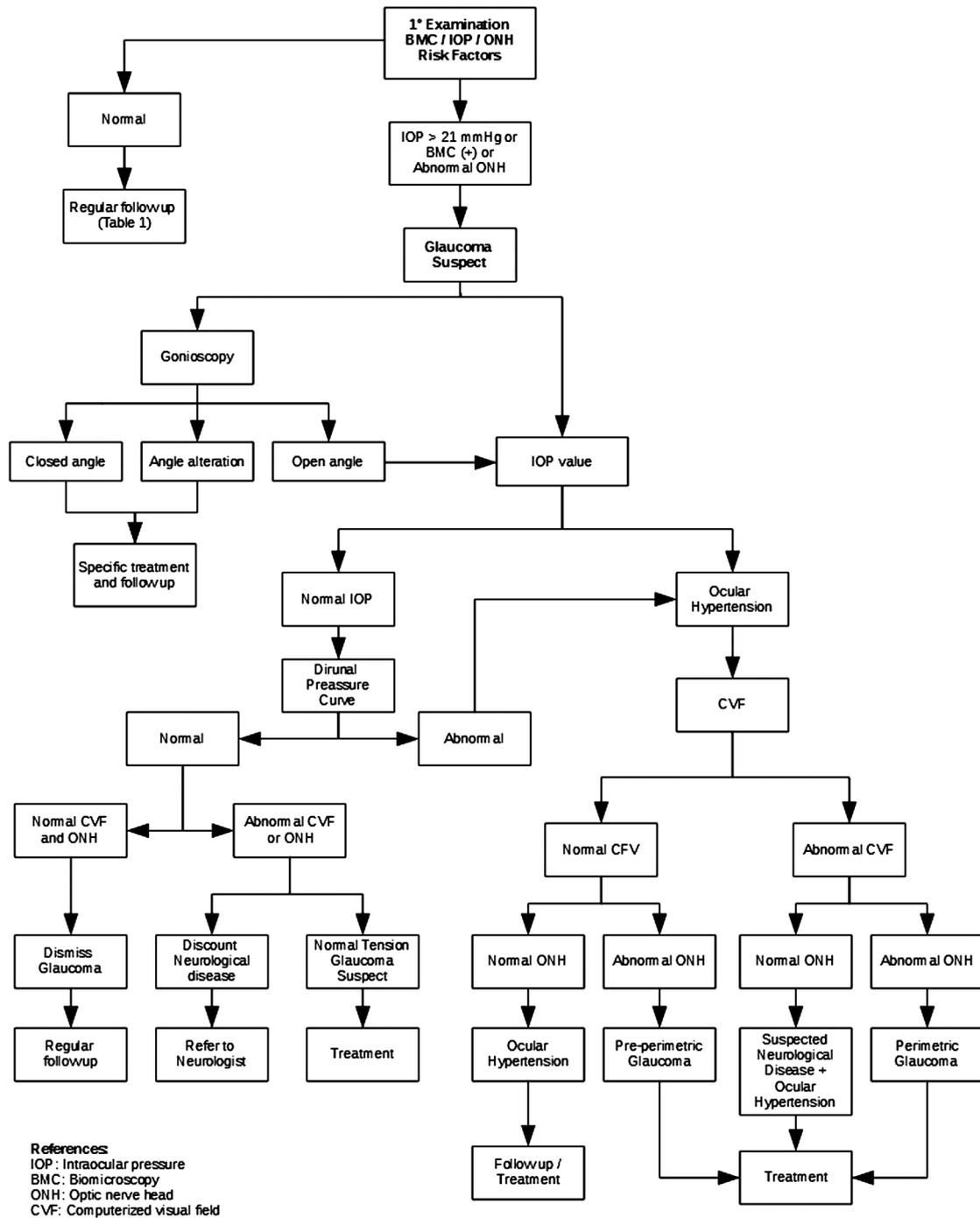


Figure 1 Critical pathway for POAG diagnosis.

patients followed up for other ocular pathologies different than POAG. Exclusion criteria were patients with established diagnosis of POAG, patients under glaucoma treatment or patients with other types of glaucoma different that POAG.

RESULTS

A total of 37 papers were selected that meet our standards of inclusion criteria. In all, we found 9 level I, 14 level II and 14 level III papers, basing each step of the pathway on the highest quality evidence possible. The critical pathway is shown in Figure 1.

Roughly, first clinical examination should be focused on detecting glaucoma suspect patients that are going to be studied

throughout the pathway. Patients that do not fulfill criteria for glaucoma suspect could be regularly followed up according to Table 1. Gonioscopy is a key element for splitting decision while it aims to differentiate open anterior chamber angle from other types of glaucoma like closed angle or patients with other angle alterations. After OH is confirmed, qualitative and quantitative analysis of ONH and retinal nerve fiber layer (RNFL) plus abnormalities in computerized visual field (CVF) represents major key steps for making decisions through the diagnosis process. This step by step model of making decisions proposed by the critical pathway ensure prompt diagnosis for POAG patients and reduce costs to the health system.

Table 1 Regular follow up

Age (a)	With risk factors	Without risk factors (a)
≥65	6-12mo	1
55-64	1-2d	1-3
40-54	1-3d	2-4
<40	2-4d	5-10

DISCUSSION

Even though some guidelines for open angle glaucoma diagnosis have been published, we believe that applying a step by step model is the best way for unify medical criteria and to reach cost-effectiveness.

Initial examination should include all the components of the comprehensive eye examination. Because screening methods for glaucoma in general population are not cost-effective, only patients considered glaucoma suspect should be studied deeper^[2-3]. For instance, glaucoma suspect patients are those with biomicroscopy abnormalities, high intraocular pressure (IOP) levels, abnormal appearance of the ONH and those with family history of glaucoma. Besides that, older age, type 2 diabetes, myopia, thinner central cornea, corneal hysteresis (CH) and corneal resistance factor, pseudoexfoliation material, low ocular perfusion pressure, African ancestry and Latino ethnicity are also known risk factors for glaucoma and should be assessed as well^[3,6-13]. Patients that not fulfill criteria to be considered glaucoma suspect are considered normal and can be followed up according to the regime showed in Table 1.

During first ophthalmological examination, detailed biomicroscopy and pupillary dilatation should be performed looking for anterior segment abnormalities, with special consideration in the presence of pseudoexfoliation syndrome (PXFS). PXFS is known to be a strong independent risk factor for glaucoma progression in patients with OH^[11]. Recent studies showed that after a mean of 8.7y without treatment, glaucoma conversion rate was twice as high in patients with OH and PXFS as in control patients (OH without PXFS)^[12]. Exfoliative glaucoma (XFG) affects up to 6 million people worldwide and is known to have higher IOP levels and greater 24h IOP fluctuations, with worse response to medical and surgical treatment and worse overall prognosis^[13].

Older age and ethnicity are well-known risk factors for glaucoma. Several epidemiological studies demonstrated a direct relationship between increasing age and the higher prevalence of glaucoma^[3,6]. In addition to this, POAG is three-fold times more frequent among Africans Americans and Hispanics ancestry compared with non-Hispanic Whites^[1,14]. Furthermore, blindness from glaucoma reaches six times more Africans Americans than Caucasian Americans patients, although there is no clear evidence if this difference lies in the individual predisposition or it represents difficulties in the access to the health system^[15].

Family history is another risk factor for glaucoma. For instance, the Rotterdam Eye Study, the Baltimore Eye Survey and the Los Angeles Latino Eye Study demonstrated that individuals with first-degree relatives with confirmed POAG have higher odds of having glaucoma^[6,10,14]. Interestingly, the odds of developing glaucoma increases as does the number of relatives with confirmed POAG.

High IOP level is a major risk factor for glaucoma. Several population-based studies provided strong evidence to consider IOP as a key element for glaucomatous optic nerve damage progression^[11,15-17]. Because there is great inter-individual variation in the susceptibility of the optic nerve to IOP-related damage, defining an IOP cutoff measure for screening and diagnosing glaucoma remains arbitrary. Nevertheless, most studies support the fact that IOP levels higher than 21 mm Hg represent a higher risk for glaucoma development and so it seems reasonable to accept that value as standard cutoff^[6,16-17].

Measurement of central corneal thickness (CCT) is an important element for glaucoma diagnosis because it represents not only an independent risk factor but also it helps the interpretation of IOP readings when corneal thickness is too distant from normal values^[3,6,10,18]. Population-based studies showed that Latinos or African Americans, whom mean CCT is 546 and 534 μm respectively, have higher glaucoma prevalence than Caucasian Americans or Asians with mean CCT of 556 and 552 μm, respectively. Hence, CCT is considered an independent risk factor for glaucoma development^[18-19]. On the other hand, IOP readings could be under or overestimated when CCT are too thin or too thick, and despite some correcting-formulas have been published, there are still none universally accepted. Finally, because IOP readings from Goldmann applanation tonometry (GAT) depends on corneal resistance to indentation and stiffness, patients with abnormal corneas like those following keratorefractive surgery, keratoconus or Fuchs endotheliopathy should be measured by methods less influenced by corneal thickness like pneumotonometry. However, it should be noted that pneumotonometry measurements are known to overestimate IOP readings when compared to GAT and those overestimations are higher as the IOP level increases^[19].

CH and corneal resistance factor, two previously unmeasured corneal biomechanical characteristics, have gained importance referring to glaucoma diagnosis and follow-up. It has been suggested that changes in corneal biomechanical factors are associated with the development and progression of glaucoma, especially in normal tension glaucoma^[10,20-21]. Recent studies demonstrated that low CH is directly associated with progressive glaucomatous optic neuropathy^[20]. Thus, CH can be used not only for screening and diagnosis purpose but also as one of the prognostic factors for glaucoma progression, independent of corneal thickness or IOP.

Patients with axial myopia are prone to develop glaucoma. Several large cross-sectional epidemiological studies showed evidence that persons with myopia have a higher prevalence of POAG than normal patients. Hypothetically, patients with axial myopia have weaker scleral support, which finally increases ONH susceptibility to glaucomatous ONH damage^[6,22-24].

Gonioscopy represents a key-decision test for glaucoma suspect patients. With gonioscopy, physicians would differentiate patients with open anterior chamber angle that will continue throughout the pathway from alternative diagnosis like angle-closure glaucoma and those patients with structural abnormalities like angle recession, peripheral anterior synechiae, angle neovascularization, pigment dispersion, and inflammatory precipitates who will need specific treatments and follow up^[25].

Patients with several risk factors for glaucoma but constantly normal IOP readings during medical examinations should be further assessed. Several ocular, hemodynamic and neurohormonal factors determine circadian variations in IOP readings in normal patients and, even more, these variations were found to be greater in patients with suspected or confirmed glaucoma^[26-27]. Measurements made with GAT during office hours capture the IOP at specific moments and therefore do not reflect IOP fluctuations over a 24h period. Thus, glaucoma suspect patients with IOP levels below 21 mm Hg need to be studied with a Diurnal Pressure Curve (DPC) in order to detect, if any, IOP peaks during the entire day^[27]. Rebound tonometry as developed by iCare (Tiolat, Helsinki, Finland) emerged as a complement for self-monitor IOP, and clinical studies have demonstrated high agreement between GAT and iCare results^[28-31]. The instrument is easy to use for IOP measurements at home, and the results are reliable after a short period of instruction and practice. Thus, iCare represents a good alternative for IOP readings after office when DPC is not practicable. In case DPC is normal (no IOP peaks are detected) and patients have no visual field or ONH alterations, glaucoma diagnosis is dismissed. If a patient has a normal DPC but there are signs of visual field or ONH alterations, normal tension glaucoma and/or neurological disease should be ruled out. Finally, those patients with abnormal DPC have confirmed OH and should continue through the critical pathway.

CVF evaluation with static threshold perimetry remains the gold standard test for glaucoma detection and follow up^[2,6]. It is important to mention that testing strategies should be individualized to patients degree of vision loss by using specific programs that evaluate the central threshold sensitivity at 24 degrees, 30 degrees, and 10 degrees, and by varying stimulus size^[6,32]. On the other hand, ONH and RNFL evaluation with both qualitative and quantitative imaging test should be performed^[2,33]. Stereoscopic disc photograph is the preferred method for evaluation and follow

up, whereas confocal scanning laser ophthalmoscopy, optical coherence tomography (OCT), and scanning laser polarimetry showed similar results to detect glaucomatous patients^[33-37]. Nevertheless, physicians should be encouraged to always use computer-based quantitative imaging test as complementary tests and evaluate the patients full context after making decisions.

The next step for splitting decisions in a glaucoma suspect patient relies on the results of both CVF and ONH. Those patients with normal CVF and ONH are considered OH patients and the decision for treating and/or follow up depends on several factors that are beyond the purpose this pathway. By the other side, those patients with OH, normal CVF but abnormal ONH are diagnosed as pre-perimetric glaucoma and should be treated^[6].

In the case of patients with high IOP readings and abnormal CVF but non glaucomatous optic nerve damage should be referred to neurologist to rule out neurological diseases. Finally, patients with OH, abnormal visual field and alteration of ONH and RNFL are diagnosed as perimetric glaucoma and should be treated^[35,37].

Even though there is no universally accepted consensus regarding glaucoma diagnosis due to its multifactorial etiology and clinical presentation, we believe that this evidence-based step by step model of making decisions improves the quality of medical attention and unify criteria.

A critical pathway, evidence-based guideline, may be a useful tool intended to reduce costs while maintaining or even improving the quality of care in the diagnosis of a highly prevalent pathology such as open angle glaucoma.

ACKNOWLEDGEMENTS

We would like to express our deepest gratitude to Dr. Carlos Bantar for his valuable collaboration in the preparation of the manuscript.

Conflicts of Interest: Allocco AR, None; Ponce JA, None; Riera MJ, None; Magurno MG, None.

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