Der Ophthalmologe

Übersichten

Ophthalmologe
https://doi.org/10.1007/s00347-021-01378-5
Accepted: 19 March 2021

Alexander K. Schuster · Felix M. Wagner · Norbert Pfeiffer · Esther M. Hoffmann

Augenklinik und Poliklinik, Universitätsmedizin Mainz, Mainz, Germany

Risk factors for open-angle glaucoma and recommendations for glaucoma screening

Learning objectives

After reading this article, you will:

- Be able to classify the frequency of the presence and occurrence of open-angle glaucoma.
- Be able to name the relevant risk factors for the development of open angle-glaucoma.
- Know quality parameters for population-based screening and be able to classify findings during screening.
- Be able to evaluate the risk factors of open-angle glaucoma for screening.

Introduction

Glaucoma is a group of slowly progressive optic neuropathies that result in loss of retinal ganglion cells and their axons, with resultant visual field defects [1]. Glaucoma can be differentiated into open-angle glaucoma and acute or chronic angle closure based on the iridocorneal angle configuration. In the latter, the chamber angle is displaced, whereas in open-angle glaucoma, it is macroscopically open.

Open-angle glaucoma often becomes symptomatic only at an advanced stage [2], making *screening* of great clinical importance. Crabb et al. report that 26% of patients initially do not notice any symptoms of their disease [2]. When respondents were asked to reproduce their visual field defect, 54% chose a sample image with blurred spots [2]. As a result, many patients do not notice the disease and no ophthalmologist is consulted. However, regular glaucoma screening allows the disease to be detected at an early stage. An Australian population-based study reports that if no eye exam has been performed in the previous 2 years, there is an eight-fold greater likelihood of undiagnosed glaucoma [3]. It is not yet possible to reverse nerve fiber loss that has already occurred or to completely reverse visual field defects. However, there are therapeutic measures that can stop or delay further progression of open-angle glaucoma in many cases [4–6].

Against this background, the Association of the Scientific Medical Societies in Germany (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften*, AWMF) guideline (S2e) of the German Ophthalmological Society (DOG) and the German Professional Association of Ophthalmologists (BVA) was created for the "Assessment of risk factors for the occurrence of open angle glaucoma" [7], from which recommendations for open-angle glaucoma screening were derived. These recommendations will be presented in this CME article; therefore, this text stays relatively close to the guideline. In particular, the recommendations/statements have been adopted from the guideline. Only individuals who are not at increased risk for open-angle glaucoma due to other eye diseases, eye surgery, and drug side effects other than the use of steroids are considered.

Epidemiology

Prevalence of open-angle glaucoma

A systematic review of population-based studies [8] reports that 2.93% of the European population aged 40–80 years has glaucoma, the majority of whom have open-angle glaucoma (prevalence of 2.51%). Data from the Gutenberg Health Study confirm these figures for the German population aged 35–74 years [9]. Prevalence estimates describe how many people have a certain disease at any one time. Estimates of *incidence*, on the other hand, indicate how many people who do not have the disease at that time will develop the disease within a certain time.

Age and gender dependency

A meta-analysis shows that open-angle glaucoma is more frequent with increasing age ([10]; **Fig. 1**). A 2.0- to 2.5-fold increase per decade of age is observed after the age of 40 years. At the age of 40 years, 0.4% of the population has open-angle glaucoma, at the age of 50 years 0.7%, at the age of 60 years 1.4%, at the age of 70 years 2.10%, at the age of 80 years 5.3%, and at the age of 90 years about 10%.

This study also shows that men are 1.3 times more likely to have open-angle glaucoma. Data from 54 population-based studies were analyzed, including ethnicity, year of study, and definition of glaucoma [10].

Statement The prevalence of open-angle glaucoma increases with age in the

The German version of this article can be found under https://doi.org/10.1007/s00347-020-01251-x

Published online: 21 April 2021

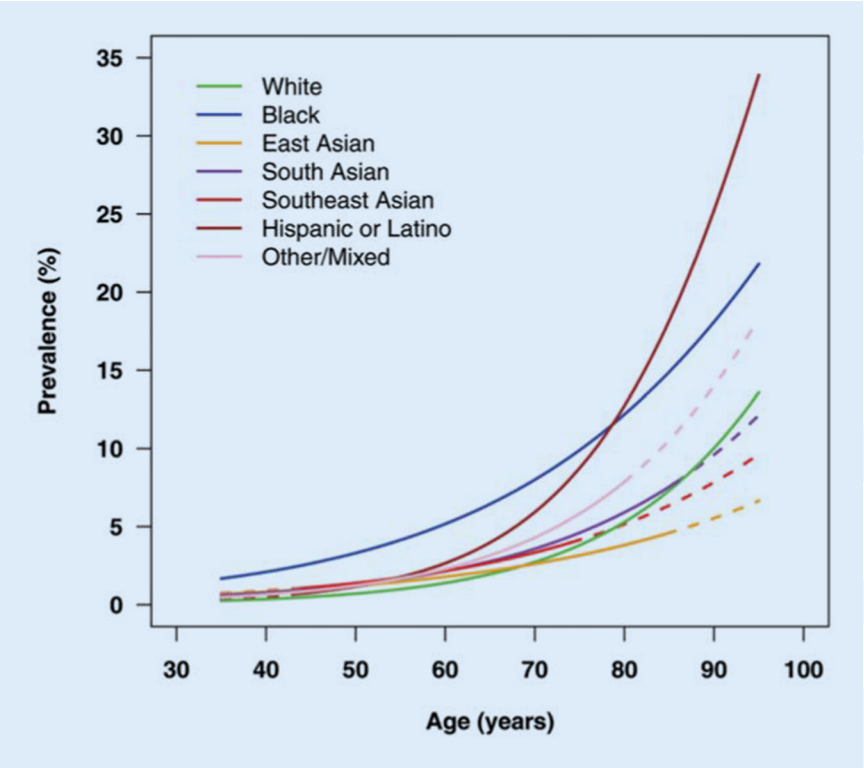

Fig. 1 ▲ Prevalence of open-angle glaucoma. (Figure from the meta-analysis by Kapetanakis et al. [10])

Caucasian population up to 10% at the age of 90 years.

Incidence of open-angle glaucoma

Studies on the occurrence of open-angle glaucoma (incidence) show that about 0.5–1.5% of people aged 40–80 years develop glaucoma within 5 years. Therefore, repeated screening tests were performed in these studies to also detect undiagnosed glaucoma. However, there are significant differences in the estimations of the incidence of open-angle glaucoma, partly due to methodological differences in the studies, such as the glaucoma definition used, the time intervals considered, and the average age of the cohorts considered. Glaucoma incidence was investigated in different primary *Caucasian cohorts* [11–17]. In the Blue Mountain Eye Study, 0.3% of subjects developed open-angle glaucoma over a 10-year period [16], and the Rotterdam Eye Study found a similar pattern with 0.6% (definite) and 1.2% (definite and probable) over 5 years, and 2.8% (definite and probable) over approximately 10 years [13, 14]. The Ponza Eye Study reports an incidence of definite open-angle glaucoma of 3.8% over a 12-year observation period [12]. In other ethnic groups, the incidence was sometimes lower and sometimes higher [18–21]. Having said that, some studies had a low response rate and a small study size. However, there is a lack of reliable data in the very elderly group (over 90 years).

Age dependence of incidence

Analogous to the prevalence, the incidence of open-angle glaucoma is age dependent. The Rotterdam Eye Study reports that the risk increases 1.07-fold per year (95% confidence interval [CI]: 1.04–1.11) [22]. The incidence of open-angle glaucoma was analyzed in a Caucasian Australian cohort: Compared to persons aged 40–49 years, the risk was two-fold higher in 50- to 59-year-olds, 8.4-fold higher in persons aged 60–69 years, 12.2-fold higher in persons aged 70–79 years, and 8.6-fold higher in persons over 80 years of age [23]. However, due to the size of the study, the estimates were imprecise, especially at higher ages. Men were 1.3–2 times more likely to develop new open-angle glaucoma at a mean observation period of 5–9 years [14, 17, 24]. This difference was small and could not be statistically proven.

Statement Between 0.5 and 1.5% of 40- to 80-year-olds will develop open-angle glaucoma within the next 5 years. The incidence increases particularly with advanced age.

Risk factors for the development of open-angle glaucoma

In addition to age, a positive family history, increased intraocular pressure, myopic refractive error, and pseudoexfoliation are risk factors for open-angle glaucoma and are associated with increased incidence.

Family history

According to a study from Sweden, a positive family history (for glaucoma) is a risk factor: People with a positive family history are two times more likely to develop glaucoma [24]. A similar result is reported by the Visual Impairment Project from Australia [23].

However, glaucoma patients report that their mothers (5.0%) and sisters (2.6%) are more likely to have glaucoma than their fathers (1.5%) and brothers (1.2%) [25]. On the other hand, epidemiological data suggest that men are more likely to have open-angle glaucoma than women [10]. This indicates that patient history data may show memory bias, survival bias, and underdiagnosis of the disease.

Statement Individuals with a positive first-degree family history have a two-fold higher risk of developing glaucoma.

Intraocular pressure

The presence of elevated intraocular pressure is associated with an increased risk for developing open-angle glaucoma. This association has been described in several population-based studies [22–24].

In the case of *increased intraocular pressure* (24–32 mm Hg) without prior

glaucomatous disease, the risk of developing glaucoma within 5 years is 9.5%, as demonstrated by the control arm of the Ocular Hypertension Treatment Study [26]. A reduction in intraocular pressure results in a reduction to 4.4% [26]. The European Glaucoma Prevention Study showed a conversion rate in ocular hypertension (22–29 mm Hg) of 13.4% with dorzolamide and 14.1% without local therapy after 5 years [27]. While the Ocular Hypertension Treatment Study [26] and the study by Ekstrom [24] used Goldmann applanation tonometry to determine intraocular pressure, the Visual Impairment Project [23] initially measured without applanation tonometry and only in the case of an increased value was the measurement confirmed using Goldmann applanation tonometry.

The reliability of *intraocular pressure measurement* (defined as transcorneal pressure) differs between different measurement methods, as does the agreement with *Goldmann applanation tonometry* [28]. Therefore, if the intraocular pressure is not measured according to Goldmann, a value of 22 mm Hg or more should be checked with Goldmann applanation tonometry.

In addition, thinner central corneal thickness in ocular hypertension is known to be a risk factor for the occurrence of open-angle glaucoma, as shown in the European Glaucoma Prevention Study [29].

Statement The risk of open-angle glaucoma increases with higher intraocular pressure. In the case of ocular hypertension (≥ 24 mm Hg), the risk of developing glaucoma within the next 5 years is 9%.

Refractive error

In the Rotterdam Eye Study, *high myopia* (–4 dpt or more) was shown to be a risk factor for the occurrence of open-angle glaucoma (2.3-fold increase) [13]. This was also shown for other ethnic groups: In a Chinese cohort study, myopia (–0.5 dpt or more) was also shown to be a risk factor for open-angle glaucoma [19]. The Chinnai Eye Disease Incidence Study showed that *axis length* is related to the risk of open-angle glaucoma: The risk increased by a factor of 1.5 per millimeter increase in axis length [21]. In addition, in highly myopic eyes, optic disc assessment is complicated by oblique optic nerve entry and, for example, a myopic conus.

Statement Myopia from –4 dpt carries a two- to three-fold higher risk of glaucoma.

Pseudoexfoliation and pigment dispersion

Three studies in Caucasians report an increased risk of glaucoma with pseudoexfoliation: This risk was higher by a factor of 4.19 [11], 4.8 [23], and 5.68 [24]. Pseudoexfoliation was diagnosed by slit-lamp microscopy. In pseudophakic eyes, however, the deposits accumulate especially at the periphery of the intraocular lens [30], which is why an *examination in mydriasis* is particularly important here. In pigment dispersion (syndrome), the risk of conversion is 10% after 5 years and 15% after 15 years [31]. Young myopic men in particular (mean age 42 years) seem to develop pigment dispersion glaucoma.

Statement Pseudoexfoliation increases the risk of open-angle glaucoma by a factor of 4–6.

Other factors associated with open-angle glaucoma

Ethnicity

Individuals with *dark skin color* have a three-fold higher risk of open-angle glaucoma compared to people with light skin color [10], and they develop the disease at an earlier age.

According to the results of two studies, people *of Latin American origin* are also more likely to develop open-angle glaucoma with increasing age, especially beyond the age of 80 years.

Note Individuals with dark skin color are three times more likely to develop open-angle glaucoma than are individuals with light skin color. A significantly steeper increase with age is seen in people of Latin American origin compared to other ethnicities.

Steroids

Oral or topical use of steroids can cause *secondary open-angle glaucoma* in predisposed patients.

Very few results are available from population-based studies on the use of steroids and the occurrence of open-angle glaucoma [32]. However, a link between *systemic steroid administration* and a possible increase in intraocular pressure has long been known from numerous clinical studies [33–35]. Glucocorticoid nasal sprays have not been shown to be associated with changes in intraocular pressure [36, 37]. No case of glaucoma was found in either review [36, 37].

However, a correlation between open-angle glaucoma/increased intraocular pressure and the use of inhaled corticosteroids in individuals with a positive family history [38] is possible, especially if the dose is increased (four puffs/day for at least 3 months).

Steroids applied topically to the eye have been shown in clinical studies to increase intraocular pressure [39], and this appears to be more common than with systemic steroid administration, leading to higher pressure levels. Myopic and high myopic patients are particularly affected by this, as observed in postoperative treatment after cataract surgery [40].

Intravitreal steroids can also increase intraocular pressure [41], in both a dose- and a drug-dependent manner. A systematic review reports that 11% of patients develop increased intraocular pressure with 0.35 mg intravitreal dexamethasone, 15% with 0.7 mg dexamethasone, 32% with 4 mg intravitreal triamcinolone, 66% with 0.59 mg fluocinolone, and 79% with 2.1 mg fluocinolone [41]. These data show a *dose-dependent steroid response*. For the lower concentration fluocinolone preparation available in Europe (0.19 mg), a study using retrospective data showed an increase in intraocular pressure (by 10 mm Hg or more) in 22% of patients [42].

Statement A higher risk for the occurrence of elevated intraocular pressure is seen with systemic, topically applied ophthalmic, and intravitreal steroids.

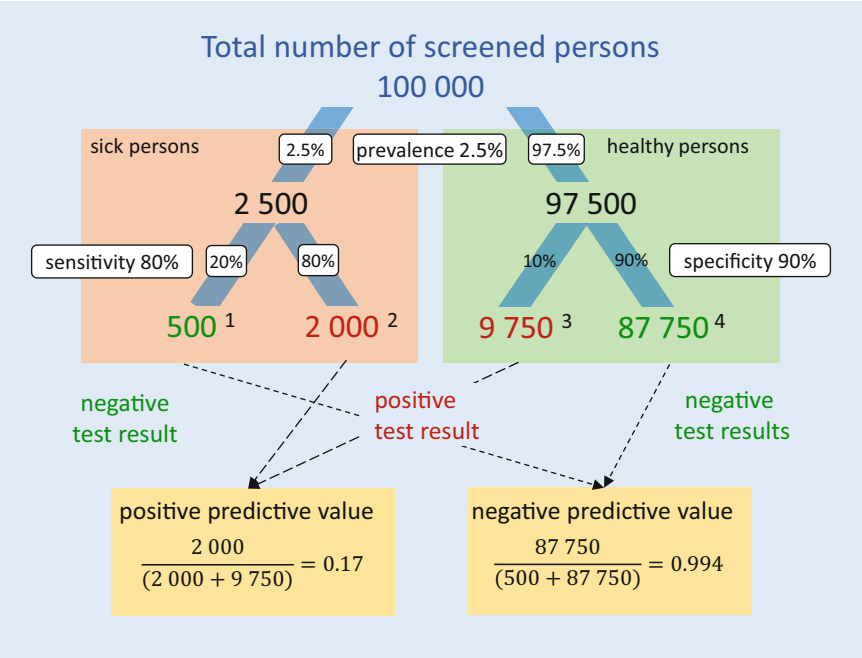

Fig. 2 ▲ Sensitivity, specificity, positive predictive value, and negative predictive value in glaucoma screening using an example (*1* false-negative, *2* true-positive, *3* false-positive, *4* true-negative test result)

Disc morphology

The *vertical optic cup–disc ratio* (CDR) is associated with a higher probability of glaucoma with increasing values. In a systematic review [43], open-angle glaucoma was 7.0–7.5 times more likely with a CDR ≥ 0.6 (compared to a CDR of 0.6), and 14 times more likely with a CDR ≥ 0.7. However, it must be taken into account that with increasing disc size, the physiological cup of the optic disc also increases and the CDR is physiologically larger [9, 44]. With a side difference of ≥ 0.2 in the vertical CDR, open-angle glaucoma is four times more likely, and with a vertical CDR ≥ 0.3 as much as seven times more likely [43]. Other morphological changes are also associated with an increased risk of open-angle glaucoma. In the presence of *optic disc hemorrhage*, open-angle glaucoma is 7.5 times more likely [45]. The most common theory for optic disc hemorrhage is mechanical vascular disruption [46], which indicates increased sensitivity of the optic disc. Other signs that have been associated with the diagnosis of glaucoma (defined by multiple expert assessments of the optic disc) include increased optic disc cupping and the presence of a rim notch and bayoneting of small vessels at the upper and lower optic disc margins. It should be noted that optic disc cupping is also a clinical sign of glaucoma and may be interpreted as an early sign of the disease.

Statement (Vertical) optic disc cupping with a CDR ≥ 0.6 in normal-sized optic discs is associated with an increased risk of glaucoma.

Statement A side difference in (vertical) optic disc cupping increases the likelihood of glaucoma (approximately four-fold for ≥ 0.2 side difference, approximately seven-fold for ≥ 0.3 side difference).

Statement The probability of glaucoma is 7.5 times higher in the case of optic disc hemorrhage.

Rationale for glaucoma screening

The vast majority of people with glaucoma notice the disease late, after functional deficits have already developed [47]. Treatment options with low side effect profiles are available, such as the use of *eye drops* that lower intraocular pressure [48] and prevent or slow the progression of glaucoma [4–6]. Therefore, glaucoma screening is deemed promising, and the expert consensus concluded [7] that patients at increased risk should be offered open-angle glaucoma screening at defined intervals.

The available evidence for *glaucoma screening* is limited, given that there are no randomized studies evaluating the extent to which—timely—glaucoma screening can actually prevent vision loss or blindness. Therefore, the evidence can only be derived indirectly and is subject to a certain degree of uncertainty. From an ethical perspective, and in the opinion of the expert committee, the consequences of glaucoma that is not detected or detected too late outweigh the consequences of suspected glaucoma that later turns out to be unfounded through additional diagnostics.

Several methods are available for glaucoma screening. When *tonometry* is used as the sole measure to diagnose glaucoma, sensitivity (percentage of people diagnosed with the test out of all people with glaucoma) and specificity (percentage of people diagnosed as healthy out of all healthy people) depend on the thresholds chosen. Chan et al. describe a sensitivity of 30% with an intraocular pressure threshold of 21 mm Hg and of 8% for a threshold of 26 mm Hg, as well as a specificity of 81% (for 21 mm Hg) to 98% (for 26 mm Hg) [49]. In fundoscopic *examination of the optic disc*, sensitivity ranges from 66 [50] to 78% [51], while specificity ranges from 60 [50] to 83% [51]. *Ophthalmoscopy* is considered to have sufficient specificity to detect glaucoma [52]. Screening based on patient history questions, which could be asked, e.g., by the primary care physician, has not been shown to be effective [52]. Other methods such as *perimetry* are highly dependent on patient cooperation [53], meaning that no reliable statements can be made about sensitivity and specificity. Newer methods such as *optical coherence tomography* (OCT) measurements of the optic disc [54] and the macula, especially the ganglion cell layer, or *deep learning algorithms* based on fundus images [55] achieve higher sensitivity and specificity than do conventional approaches under

Table 1 Risk factors relevant to screening intervals according to the guideline "Risk factors for open-angle glaucoma" [7]

Risk factors for shortening the examination interval
Family predisposition (first-degree relative)
Myopia from 4 dpt
People with dark skin color or of Latin American descent
Ocular hypertension with intraocular pressure of 22–25 mm Hg (pachymetry-controlled)
Borderline optic disc cupping (vertical CDR ≥ 0.6)
Side difference of optic disc cupping (vertical CDR ≥ 0.2)
Prolonged treatment with steroids systemically or in the eye

CDR cup–disc ratio

study conditions. However, imaging diagnostics for glaucoma (OCT, etc.) represent individual health care services in Germany and are not included in the service catalog of statutory health insurances.

If intraocular pressure measurement is combined with *binocular indirect ophthalmoscopy* to test for the presence of glaucoma, studies show a sensitivity of 64% at a specificity of 96% (individuals with intraocular pressure below 18 mm Hg were defined as healthy) [56] and a sensitivity of 61% at a specificity of 84% (with a defined pressure threshold of 21 mm Hg and vertical CDR ≥ 0.5). However, fixed intraocular pressure thresholds should be viewed critically, especially in the context of normal-tension glaucoma. The expert consensus of this guideline recommends at least a combination of intraocular pressure measurement and binocular indirect ophthalmoscopy for glaucoma screening [7].

However, binocular indirect ophthalmoscopy as part of the screening procedure requires sound experience in disc evaluation in order to avoid too many false-positive findings. Therefore, in equivocal cases, imaging, especially with modern OCT technology, and a *visual field examination* are recommended for further clarification. In a recent study on glaucoma detection, a sensitivity of 77% and a specificity of 98% could be achieved by combining OCT and visual field findings, without taking into account the respective intraocular pressure [57].

However, it is also important that the combination of intraocular pressure measurement and optic disc assessment is additionally able to identify individuals with *ocular hypertension.*

Statement The glaucoma screening examination should include at least a binocular examination of the optic disc and intraocular pressure measurement. These examinations represent only a minor burden for the patient.

Patients need to be educated about the benefits and risks of glaucoma screening as well as the typically long asymptomatic course of glaucoma disease, which is characterized by irreversible nerve fiber loss. In addition, it should be explained to patients that an abnormal result in screening does not necessarily mean that the disease is actually present, but that further examinations (perimetry, pachymetry, repeated intraocular pressure measurements, morphometric imaging) are required to confirm or rule out the suspicion. The result may also indicate ocular hypertension, which, although not requiring treatment, must be monitored more closely and intensively than in patients with a negative examination result.

The *positive predictive value* indicates how many people with a positive test result actually have the disease (e.g., in the 60- to 64-year-old age group, only 17 out of 100 individuals with abnormal findings have glaucoma with an assumed sensitivity of 80% and a specificity of 90%; **Fig. 2**). The percentage of undetected glaucoma is comparatively low due to the low prevalence: 6 out of 1000 persons with a negative test result have glaucoma at the age of 60–64 years that was not detected (assumed sensitivity of 80%, specificity of 90%, and prevalence of 2.5% in the given example). It is important to note that a single tonometric measurement does not rule out ocular hypertension due to the fluctuation in measured values [58].

Statement Patient education on the benefits and risks of glaucoma screening should be provided. The patient should also be informed about the further procedure in the case of a positive result.

Note Due to the fluctuation in tonometry values, a single tonometric measurement does not exclude ocular hypertension or glaucoma.

The expert consensus in the guideline [7] advocated that *risk groups* in particular should be more closely monitored. These risk groups are determined by factors that increase the risk of developing glaucoma at least two-fold. Risk factors that increase the risk less than two-fold (e.g., gender) are therefore not considered. These risk factors include: First-degree family history of glaucoma, myopia of –4 dpt or more, individuals with dark skin or of Latin American descent, ocular hypertension with intraocular pressure of 22–25 mm Hg (pachymetry-controlled), borderline optic disc cupping (vertical CDR ≥ 0.6), side difference in optic disc cupping (vertical CDR ≥ 0.2), and prolonged systemic or topical steroid eye treatment (**Table 1**). After the start of steroid medication, steroid response should be ruled out by timely intraocular pressure monitoring.

Note Untreated glaucoma progresses at different rates. This should be taken into account when determining the intervals at which glaucoma examinations are performed.

The prevalence and incidence of open-angle glaucoma increases with *age.* To date, however, there is little epidemiological data on open-angle glaucoma in people under 40 years of age. Therefore, no evidence-based statement can be made for this age group. However, if risk factors are present, an examination should also be considered in individuals aged 40 years.

Glaucoma screening at a younger age (40–60 years) is important, since the disease can result in a reduced *ability to drive*;

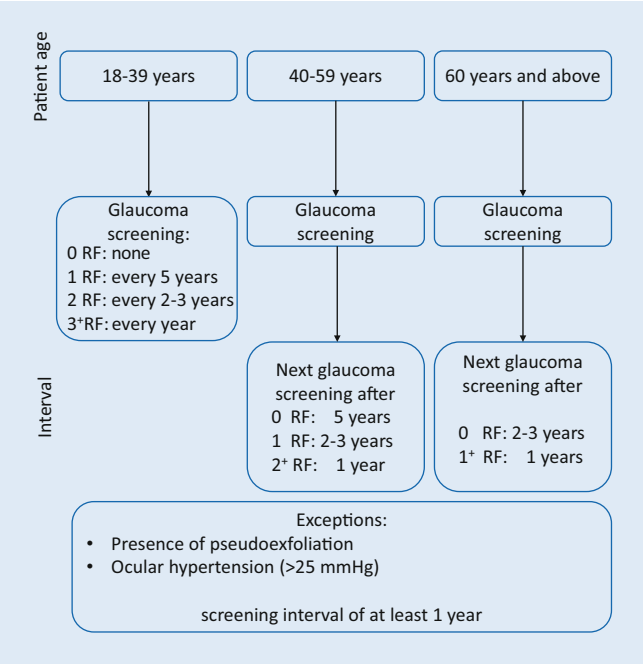

Fig. 3 ◂ Recommendations for glaucoma screening (*RF* risk factors other than age, + includes this or a higher number of risk factors)

for example, Gramer et al. report that 10–20% of patients were not fit to drive at the time of first presentation in clinics due to an impaired binocular visual field [59]. In addition, a glaucoma patient with visual impairment or blindness at a young age lives longer with this disability than does someone who becomes ill at an advanced age.

However, there is a lack of studies from which it can be reliably deduced for whom glaucoma screening offers more advantages than disadvantages and from what age such an examination should be performed. Therefore, based on clinical experience and a risk–benefit assessment by the editorial committee of the guideline, it is recommended that glaucoma screening should be offered to all persons over the age of 40 years.

Note From the age of 40, everyone should be offered glaucoma screening.

To date, there is no literature on how *examination intervals* should be set for high-risk patients. Since the rate of progression of glaucomatous disease can vary widely [1], this must also be taken into account when setting intervals for repeat examinations. The intervals must be long enough to detect a slow average progression of the disease while at the same time short enough to detect a rapidly progressive form of the disease before severe functional impairment occurs. Here, too, there is a lack of studies from which the interval length can be reliably derived. The expert consensus of this guideline therefore recommends [7] that the interval length should be determined according to risk factors for the occurrence of open-angle glaucoma and age.

If there are no risk factors other than age, the examination interval should be 5 years at the age of 40–59 and 2–3 years from the age of 60 (**Fig. 3**). At an assumed sensitivity of 80% and a specificity of 90% for the examination, this leads to a negative predictive value (persons with negative findings [no open-angle glaucoma] also do not have open-angle glaucoma) of over 99%. However, the positive predictive value showed a high percentage of false positives: At the age of 40–49 years, only one in 20 persons with positive findings have open-angle glaucoma after 5 years; at the age of over 70 years, only one in eight persons with positive findings have open-angle glaucoma after 2.5 years. The patient needs to be informed about this and a positive result must be confirmed or excluded as open-angle glaucoma by further diagnostics (OCT examination, perimetry, etc.). Only by means of further examinations (imaging procedures such as OCT and visual field examination) can this high false-positive number of cases be sufficiently reduced [57].

Statement Between the ages of 40 and 59 years, examination intervals should be 5 years, and from the age of 60 onwards, 2–3 years if there are no risk factors other than age.

Due to the increased prevalence and incidence of open-angle glaucoma for the risk factors described above, the expert group is of the opinion that in persons with one risk factor (except age), the examination interval should be reduced to 2–3 years for the 40- to 59-year age group and to 1 year for persons older than 60 years [7]. In the presence of two or more risk factors (except age), the examination interval should also be reduced to 1 year for the 40- to 59-year age group [7].

Statement If there is an additional risk factor (other than age), the screening interval can be reduced to:

- 2–3 years for persons aged 40–59 years
- 1 year from 60 years.

For two or more risk factors (except age), the interval should be reduced to 1 year.

Adults under the age of 40 years should be examined every 5 years if any of the above risk factors are present, every 2–3 years if two risk factors are present, and annually if three or more risk factors are present. Glaucoma screening is also recommended for individuals with dark skin color from the age of 30 years. Again, since there are no studies from which this can be reliably deduced, the recommendation was made on the basis of expert consensus.

Note Glaucoma screening should be performed every 5 years in adults under the age of 40 years with one risk factor, every 2–3 years with two risk factors, and annually with three or more risk factors.

The *main risk factors* with the highest effect estimates for open-angle glaucoma were pseudoexfoliation and ocular hypertension with an intraocular pressure over 25 mm Hg as measured by applanation tonometry (**Table 2**). Therefore, in the presence of pseudoexfoliation or

Table 2 Risk factors that require at least annual screening according to the guideline "Risk factors for open-angle glaucoma" [7]

Risk factors that require at least one annual examination
Presence of pseudoexfoliation
Ocular hypertension with an intraocular pressure on applanation tonometry over 25 mm Hg

ocular hypertension, a screening interval of at least 1 year is recommended [7].

Statement In the presence of pseudoexfoliation or ocular hypertension with an intraocular pressure over 25 mm Hg as measured on applanation tonometry, screening should be performed at least once a year.

Patients at increased risk for open-angle glaucoma must be informed about this risk, as well as the paucity of subjective symptoms of this disease. According to the guideline, repeat screening should be recommended after the abovementioned intervals and documented accordingly. Thus, the risk of reduced quality of life, e.g., as a result of unfitness to drive due to visual field defects, can be reduced by early detection and treatment of the disease.

Statement Patients with risk factor(s) should be informed about their increased risk of glaucoma, and repeat screening at the appropriate interval should be recommended and documented.

Practical conclusion

- In the context of development of the guidelines, risk factors for open-angle glaucoma were demonstrated by the literature review.
- According to the expert consensus, these should be taken into account in the recommendations for glaucoma screening in order to implement them in a risk-adjusted manner.

Corresponding address

Univ.-Prof. Dr. med. Alexander K. Schuster
Augenklinik und Poliklinik, Universitätsmedizin Mainz
Langenbeckstr. 1, 55131 Mainz, Germany
alexander.schuster@uni-mainz.de

Acknowledgements. The authors would like to thank the editorial committee of the guideline on "Assessment of risk factors for the occurrence of open-angle glaucoma" (Prof. Dr. B. Bertram, Dr. D. Claessens, Prof. Dr. T. Dietlein, Prof. Dr. C. Erb, Prof. Dr. R. Burk, Prof. Dr. T. Klink, Prof. Dr. T. Reinhard, A. Ostrowski, Prof. Dr. N. Pfeiffer, Prof. Dr. E. Hoffmann, Prof. Dr. A. Schuster). Only on the basis of this guideline could this CME article be created.

Declarations

Conflict of interest. A.K. Schuster: A. Financial interests: Research funding at personal disposal: Allergan, Novartis, Bayer Vital (financial support for research), Heidelberg Engineering, PlusOptix (equipment). B. Non-financial interests: Endowed professorship in ophthalmological care research, donated by the Stiftung Auge and financed by DOG and BVA, Eye Clinic and Polyclinic University Medicine Mainz. Memberships: DOG, BVA, EGS, Euretina, ARVO. F.M. Wagner: A. Financial interests: F. Wagner states that there is no financial conflict of interest. B. Non-financial interests: Assistant physician at the University Eye Hospital Mainz, Mainz. Memberships: DOG, BVA, DGII, ESCRS. N. Pfeiffer: A. Financial interests: Research funding at personal disposal: Allergan, Alcon, Boehringer Ingelheim, Aerie, Santen, Novartis, further education funding. Speaker's fee or reimbursement of costs as passive participant: Santen, Novartis, Aerie, Allergan. Paid advisor/internal training reference/salary recipient or similar: Allergan, Aerie, Santen, Novartis. B. Non-financial interests: Director of the Eye Clinic and Polyclinic of the University Medical Center Mainz. Memberships: DOG, BVA, ARVO, American Academy of Ophthalmology, European Glaucoma Society, Glaucoma Research Society. E.M. Hoffmann: A. Financial interests: Speaker's fee or reimbursement as passive participant: Santen, Pharm-Allergan, Heidelberg Engineering, Novartis, MEyeTech. Paid consultant/internal training reference/salary recipient or similar: Santen, Pharm-Allergan, Heidelberg Engineering, Novartis, MEyeTech. B. Non-financial interests: Senior Physician at the Eye Clinic and Policlinic of the University Medical Center Mainz of the Johannes Gutenberg University Mainz, Head of the Department of Glaucoma Diseases of the Eye Clinic and Policlinic of the University Medical Center Mainz, Head of the Pediatric Glaucoma Center at the Eye Clinic and Policlinic of the University Medical Center Mainz. Memberships: DOG, BVA, EGS.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case.

The supplement containing this article is not sponsored by industry.

References

1. European Glaucoma Society (2014) Terminology and guidelines for glaucoma, 4 edn. PubliComm, Savona
2. Crabb DP, Smith ND, Glen FC et al (2013) How does glaucoma look?: patient perception of visual field loss. Ophthalmology 120:1120–1126
3. Weih LM, Nanjan M, Mccarty CA et al (2001) Prevalence and predictors of open-angle glaucoma: results from the visual impairment project. Ophthalmology 108:1966–1972
4. Garway-Heath DF, Crabb DP, Bunce C et al (2015) Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial. Lancet 385:1295–1304
5. Leske MC, Heijl A, Hussein M et al (2003) Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol 121:48–56
6. Leske MC, Heijl A, Hyman L et al (2007) Predictors of long-term progression in the early manifest glaucoma trial. Ophthalmology 114:1965–1972
7. Deutsche Ophthalmologische Gesellschaft (2020) Deutsche Ophthalmologische Gesellschaft (DOG), Berufsverband der Augenärzte Deutschlands e. V. BVA, Bewertung von Risikofaktoren für das Auftreten des Offenwinkelglaukoms. Leitlinie von DOG und BVA. Ophthalmologe https://doi.org/10.1007/s00347-020-01169-4
8. Tham YC, Li X, Wong TY et al (2014) Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology 121:2081–2090
9. Hohn R, Nickels S, Schuster AK et al (2018) Prevalence of glaucoma in Germany: results from the Gutenberg Health Study. Graefes Arch Clin Exp Ophthalmol 256:1695–1702
10. Kapetanakis VV, Chan MP, Foster PJ et al (2016) Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. Br J Ophthalmol 100:86–93
11. Astrom S, Stenlund H, Linden C (2007) Incidence and prevalence of pseudoexfoliations and open-angle glaucoma in northern Sweden: II. Results after 21 years of follow-up. Acta Ophthalmol Scand 85:832–837
12. Cedrone C, Mancino R, Ricci F et al (2012) The 12-year incidence of glaucoma and glaucoma-related visual field loss in Italy: the Ponza eye study. J Glaucoma 21:1–6
13. Czudowska MA, Ramdas WD, Wolfs RC et al (2010) Incidence of glaucomatous visual field loss: a ten-year follow-up from the Rotterdam Study. Ophthalmology 117:1705–1712
14. De Voogd S, Ikram MK, Wolfs RC et al (2005) Incidence of open-angle glaucoma in a general elderly population: the Rotterdam Study. Ophthalmology 112:1487–1493
15. Hitzl W, Stollinger M, Grabner G et al (2006) The Salzburg-Moorfields Collaborative Glaucoma Study: first results of the prevalence and 5-year incidences in this prospective, population-based longitudinal study. Klin Monatsbl Augenheilkd 223:970–973
16. Kawasaki R, Wang JJ, Rochtchina E et al (2013) Retinal vessel caliber is associated with the 10-year incidence of glaucoma: the Blue Mountains Eye Study. Ophthalmology 120:84–90
17. Mukesh BN, Mccarty CA, Rait JL et al (2002) Five-year incidence of open-angle glaucoma:

the visual impairment project. Ophthalmology 109:1047–1051
18. Leske MC, Wu SY, Honkanen R et al (2007) Nine-year incidence of open-angle glaucoma in the Barbados Eye Studies. Ophthalmology 114:1058–1064
19. Pan CW, Yang WY, Hu DN et al (2017) Longitudinal cohort study on the incidence of primary open-angle glaucoma in Bai Chinese. Am J Ophthalmol 176:127–133
20. Varma R, Wang D, Wu C et al (2012) Four-year incidence of open-angle glaucoma and ocular hypertension: the Los Angeles Latino Eye Study. Am J Ophthalmol 154:315–325.e311
21. Vijaya L, Rashima A, Panday M et al (2014) Predictors for incidence of primary open-angle glaucoma in a South Indian population: the Chennai eye disease incidence study. Ophthalmology 121:1370–1376
22. Ramdas WD, Wolfs RC, Hofman A et al (2011) Ocular perfusion pressure and the incidence of glaucoma: real effect or artifact? The Rotterdam Study. Invest Ophthalmol Vis Sci 52:6875–6881
23. Le A, Mukesh BN, Mccarty CA et al (2003) Risk factors associated with the incidence of open-angle glaucoma: the visual impairment project. Invest Ophthalmol Vis Sci 44:3783–3789
24. Ekstrom C (2012) Risk factors for incident open-angle glaucoma: a population-based 20-year follow-up study. Acta Ophthalmol 90:316–321
25. Mitchell P, Rochtchina E, Lee AJ et al (2002) Bias in self-reported family history and relationship to glaucoma: the Blue Mountains Eye Study. Ophthalmic Epidemiol 9:333–345
26. Kass MA, Heuer DK, Higginbotham EJ et al (2002) The ocular hypertension treatment study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 120:701–713 (discussion 829–730)
27. Miglior S, Zeyen T, Pfeiffer N et al (2005) Results of the European Glaucoma Prevention Study. Ophthalmology 112:366–375
28. Cook JA, Botello AP, Elders A et al (2012) Systematic review of the agreement of tonometers with Goldmann applanation tonometry. Ophthalmology 119:1552–1557
29. Miglior S, Pfeiffer N, Torri V et al (2007) Predictive factors for open-angle glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study. Ophthalmology 114:3–9
30. Reiter C, Gramer E, Gramer G (2012) Pseudoexfoliation syndrome: no central zone of pseudoexfoliation material in patients with pseudophakia—a clinical study. Klin Monatsbl Augenheilkd 229:241–245
31. Siddiqui Y, Ten Hulzen RD, Cameron JD et al (2003) What is the risk of developing pigmentary glaucoma from pigment dispersion syndrome? Am J Ophthalmol 135:794–799
32. Marcus MW, Muskens RP, Ramdas WD et al (2012) Corticosteroids and open-angle glaucoma in the elderly: a population-based cohort study. Drugs Aging 29:963–970
33. Alfano JE (1963) Changes in the intraocular pressure associated with systemic steroid therapy. Am J Ophthalmol 56:245–247
34. Armaly MF (1963) Effect of corticosteroids on Intraocular pressure and fluid dynamics. I. The effect of dexamethasone in the normal eye. Arch Ophthalmol 70:482–491
35. Bernstein HN, Schwartz B (1962) Effects of long-term systemic steroids on ocular pressure and tonographic values. Arch Ophthalmol 68:742–753
36. Ahmadi N, Snidvongs K, Kalish L et al (2015) Intranasal corticosteroids do not affect intraocular pressure or lens opacity: a systematic review of controlled trials. Rhinology 53:290–302
37. Valenzuela CV, Liu JC, Vila PM et al (2019) Intranasal corticosteroids do not lead to ocular changes: a systematic review and meta-analysis. Laryngoscope 129:6–12
38. Mitchell P, Cumming RG, Mackey DA (1999) Inhaled corticosteroids, family history, and risk of glaucoma. Ophthalmology 106:2301–2306
39. Becker B, Mills DW (1963) Corticosteroids and intraocular pressure. Arch Ophthalmol 70:500–507
40. Chang DF, Tan JJ, Tripodis Y (2011) Risk factors for steroid response among cataract patients. J Cataract Refract Surg 37:675–681
41. Kiddee W, Trope GE, Sheng L et al (2013) Intraocular pressure monitoring post intravitreal steroids: a systematic review. Surv Ophthalmol 58:291–310
42. Augustin AJ, Bopp S, Fechner M et al (2020) Three-year results from the retro-IDEAL study: real-world data from diabetic macular edema (DME) patients treated with ILUVIEN(®) (0.19 mg fluocinolone acetonide implant). Eur J Ophthalmol 30:382–391
43. Hollands H, Johnson D, Hollands S et al (2013) Do findings on routine examination identify patients at risk for primary open-angle glaucoma? The rational clinical examination systematic review. JAMA 309:2035–2042
44. Crowston JG, Hopley CR, Healey PR et al (2004) The effect of optic disc diameter on vertical cup to disc ratio percentiles in a population based cohort: the Blue Mountains Eye Study. Br J Ophthalmol 88:766–770
45. Gupta P, Zhao D, Guallar E et al (2016) Prevalence of Glaucoma in the United States: The 2005–2008 National Health and Nutrition Examination Survey. Invest Ophthalmol Vis Sci 57:2905–2913
46. Kim KE, Park KH (2017) Optic disc hemorrhage in glaucoma: pathophysiology and prognostic significance. Curr Opin Ophthalmol 28:105–112
47. Deva NC, Insull E, Gamble G et al (2008) Risk factors for first presentation of glaucoma with significant visual field loss. Clin Exp Ophthalmol 36:217–221
48. Li T, Lindsley K, Rouse B et al (2016) Comparative effectiveness of first-line medications for primary open-angle glaucoma: a systematic review and network meta-analysis. Ophthalmology 123:129–140
49. Chan MPY, Broadway DC, Khawaja AP et al (2017) Glaucoma and intraocular pressure in EPIC-Norfolk Eye Study: cross sectional study. BMJ 358:j3889
50. Vessani RM, Moritz R, Batis L et al (2009) Comparison of quantitative imaging devices and subjective optic nerve head assessment by general ophthalmologists to differentiate normal from glaucomatous eyes. J Glaucoma 18:253–261
51. Abrams LS, Scott IU, Spaeth GL et al (1994) Agreement among optometrists, ophthalmologists, and residents in evaluating the optic disc for glaucoma. Ophthalmology 101:1662–1667
52. Wang F, Tielsch JM, Ford DE et al (1998) Evaluation of screening schemes for eye disease in a primary care setting. Ophthalmic Epidemiol 5:69–82
53. Katz J, Sommer A (1990) Screening for glaucomatous visual field loss. The effect of patient reliability. Ophthalmology 97:1032–1037
54. Michelessi M, Li T, Miele A et al (2020) Accuracy of optical coherence tomography for diagnosing glaucoma: an overview of systematic reviews. Br J Ophthalmol. https://doi.org/10.1136/bjophthalmol-2020-316152
55. Liu H, Li L, Wormstone IM et al (2019) Development and validation of a deep learning system to detect glaucomatous optic neuropathy using fundus photographs. JAMA Ophthalmol 137:1353–1360
56. Tuck MW, Crick RP (1997) The cost-effectiveness of various modes of screening for primary open angle glaucoma. Ophthalmic Epidemiol 4:3–17
57. Iyer JV, Boland MV, Jefferys J et al (2020) Defining glaucomatous optic neuropathy using objective criteria from structural and functional testing. Br J Ophthalmol. https://doi.org/10.1136/bjophthalmol-2020-316237
58. Rotchford AP, Uppal S, Lakshmanan A et al (2012) Day-to-day variability in intraocular pressure in glaucoma and ocular hypertension. Br J Ophthalmol 96:967–970
59. Gramer G, Gramer E (2018) Stage of visual field loss and age at diagnosis in 1988 patients with different glaucomas: implications for glaucoma screening and driving ability. Int Ophthalmol 38:429–441