

Primary Angle-Closure Glaucoma: Pathophysiology, Diagnostic Approaches, and Management Strategies – A Narrative Review

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Background: Primary angle-closure glaucoma (PACG) is a major cause of irreversible blindness worldwide, particularly in Asian populations. It represents the most severe form of primary angle-closure disease (PACD) and is characterized by obstruction of the anterior chamber angle, leading to elevated intraocular pressure (IOP) and glaucomatous optic neuropathy. PACG is often asymptomatic in early stages, resulting in delayed diagnosis and management. The article reviews the epidemiology, risk factors, pathophysiology, diagnostic approaches, and management strategies of primary angle-closure glaucoma.

Methods: This narrative review was conducted through a comprehensive literature search using PubMed, Scopus, Web of Science, Google Scholar, and ResearchGate. English-language articles published between 2018 and 2025 with available full texts were included. Additional studies were identified through cross-referencing.

Results: The global prevalence of PACG is increasing, with projections indicating a significant rise by 2040. Key risk factors include advancing age, female gender, Asian ethnicity, hyperopia, shallow anterior chamber depth, short axial length, and a thick, anteriorly positioned lens. The primary mechanisms involved in pathophysiology include pupillary block and anterior displacement of the iris, resulting in angle closure and increased IOP. Diagnosis is based on clinical evaluation, including patient history, intraocular pressure measurement, gonioscopy, and assessment of the anterior chamber angle. Imaging modalities such as ultrasound biomicroscopy and anterior segment optical coherence tomography improve diagnostic precision.

Conclusion: PACG remains a public health concern due to its high risk of blindness and frequent underdiagnosis. Early detection, appropriate diagnostic evaluation, and timely intervention are essential for reducing disease burden and preventing visual impairment.

Keywords: Primary angle-closure glaucoma; intraocular pressure; anterior chamber angle; pathophysiology; risk factors; gonioscopy; epidemiology; diagnosis; management; glaucomatous optic neuropathy

Introduction

Glaucoma is a multifactorial disease caused by increased intraocular pressure (IOP), leading to visual field impairment and optic nerve pathology. High IOP increases hydrodynamic load on the optic disc, gradually resulting in its

atrophy. Glaucoma is one of the leading causes of irreversible blindness worldwide (1). It is defined as a group of optic neuropathies characterized by structural changes at the optic nerve head, leading to the death of retinal

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ganglion cells and their axons, resulting in visual field loss and blindness (2,3).

Primary angle-closure glaucoma (PACG) is a cause of blindness globally, particularly in Asian populations, where it accounts for approximately 25% of glaucoma cases (4). It represents the most severe form of primary angle-closure disease (PACD), a spectrum of disorders characterized by appositional or synechial closure of the anterior chamber angle (ACA) by the peripheral iris. This process impairs aqueous humor outflow through the trabecular meshwork (TM), resulting in elevated intraocular pressure (IOP), a major risk factor for glaucomatous optic neuropathy (5).

PACG occurs when the anterior chamber angle becomes obstructed, preventing the drainage of aqueous humor. This obstruction leads to increased intraocular pressure (IOP), which can damage the optic nerve and result in progressive vision loss (6). The disease is often asymptomatic in its early stages and typically presents with visual field defects in advanced stages unless IOP is reduced in time. A narrow anterior chamber angle or closed iridocorneal angle is a characteristic feature of this condition and is primarily diagnosed by gonioscopy (7).

Despite its significant contribution to global blindness, PACG remains underdiagnosed and is frequently identified only at advanced stages due to its asymptomatic course in the early phase. Additionally, variations in clinical presentation, anatomical predisposition, and limited access to appropriate diagnostic tools in many regions further complicate timely detection. With the global burden of glaucoma expected to rise substantially due to population aging and increased life expectancy, the impact of PACG on visual morbidity is anticipated to grow correspondingly.

In recent years, advances in diagnostic modalities, including imaging techniques such as anterior segment optical tomography and ultrasound biomicroscopy, have improved the

understanding and detection of angle-closure mechanisms. Evolving management strategies aimed at early intervention and disease prevention highlight the need for a clear, up-to-date synthesis of current evidence.

Therefore, this review was conducted to provide a comprehensive, up-to-date overview of the epidemiology, pathophysiology, risk factors, diagnostic approach and management strategies for PACG. By recent findings, this review aims to enhance clinical awareness, facilitate early diagnosis, and support effective management to reduce the burden of vision loss associated with this condition.

Material and methods

This review was conducted using a structured approach consistent with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and reproducibility.

Search Strategy

A comprehensive literature search was performed using electronic databases including PubMed, Scopus, Web of Science, Google Scholar, and ResearchGate. The following keywords and their combinations were used: "primary angle-closure glaucoma (PACG), glaucoma epidemiology, pathophysiology, risk factors, diagnosis, and management." Boolean operators (AND, OR) were applied to refine the search results.

Eligibility Criteria

Studies were included if they met the following criteria:

- English-language articles
- Published between 2018 and 2025
- Full-text articles available
- Studies addressing epidemiology, risk factors, pathophysiology, diagnosis, or management of PACG

Studies were excluded if they:

- Were not written in English
- Had no accessible full text
- Were unrelated to PACG or lacked relevant clinical information

Study Selection Process

All identified records were screened based on titles and abstracts. Relevant articles were further assessed for eligibility through full-text evaluation. Duplicate records were removed during the screening process. Additional studies were identified through manual cross-referencing of reference lists of selected articles. After the screening and eligibility assessment, 28 studies were included in the final review.

Data Extraction and Synthesis

Data from the included studies were extracted and organized into key domains: epidemiology, risk factors, pathophysiology, diagnostic methods, and management strategies. The findings were qualitatively synthesized to provide a comprehensive narrative overview of PACG.

Epidemiology

Primary angle-closure glaucoma (PACG) is a leading cause of blindness worldwide and is more common in women and individuals from East Asia. Despite its relatively high prevalence, it remains underdiagnosed (7,8). Glaucoma is one of the major causes of irreversible blindness worldwide and is considered the second leading cause of global blindness. The global burden of glaucoma has been increasing steadily over the years. It was estimated that approximately 65 million individuals were affected in 2013, which increased to around 76 million in 2020. Furthermore, projections suggest that the number of people with glaucoma may reach nearly 112 million by 2040 due to population growth and aging (1, 9-12).

Studies have shown that eyes with PACG have higher rates of blindness compared to those with primary open-angle glaucoma (POAG). The prevalence of PACG and associated blindness varies among racial and ethnic groups (1). PACG has been reported to affect more than 17 million individuals worldwide and is recognized as a major public health challenge, particularly in Asian populations. The higher burden in these populations is often attributed to anatomical predisposition, including shallower anterior chamber depth, shorter axial length, and thicker crystalline lenses. The prevalence of PACG varies across populations due to differences in age, sex, and geographical location. Research indicates that ethnicity, increasing age, and female sex are significant factors in the development of PACG (2).

In addition to anatomical and demographic variations, genetic susceptibility has also been implicated in the development of PACG, with familial aggregation observed in some populations. Regional disparities in healthcare access, awareness levels, and availability of diagnostic facilities further contribute to differences in disease detection and reported prevalence. In many low- and middle-income countries, limited screening programs and inadequate eye care infrastructure result in delayed diagnosis, often when significant optic nerve damage has already occurred.

The prevalence of primary angle-closure glaucoma (PACG) is expected to increase by approximately 50% by the year 2040, and it continues to be a major contributor to visual impairment and blindness worldwide (13,14). This increasing trend is closely linked to population aging, urbanization, and improved life expectancy, all of which increase the proportion of individuals at risk for age-related anatomical changes that predispose to angle closure.

Gender differences are also evident in glaucoma. Men are noted to be at higher risk for POAG, whereas women are at higher risk for PACG (15,10). This difference may be associated with anatomical variations such as shallower anterior chambers and smaller ocular dimensions in females, which increase susceptibility to angle closure.

Overall, PACG represents a significant and growing health concern with a disproportionate impact on populations. The combination of demographic shifts, anatomical predisposition, genetic factors, and healthcare disparities contributes to its pattern. Strengthening awareness, implementing targeted screening strategies, and improving early diagnostic services are essential to reduce the burden of PACG-related visual impairment and blindness.

Risk factors

The development of primary angle-closure glaucoma (PACG) is multifactorial, involving demographic, anatomical, refractive, and genetic factors. These factors contribute to anterior segment crowding, narrowing of the anterior chamber angle, and impaired aqueous humor outflow, predisposing individuals to elevated intraocular pressure and glaucomatous optic neuropathy. Understanding these risk factors is essential for early identification of high-risk individuals, timely screening, and prevention of disease progression.

Age

The prevalence of primary angle-closure glaucoma (PACG) increases with advancing age (16). This is mainly due to progressive thickening of the crystalline lens and a reduction in anterior chamber depth, which leads to crowding of the anterior segment and narrowing of the anterior chamber angle.

Asian descent

Individuals of Asian origin are at a higher risk of PACG (10,13,17,18). This is attributed to anatomical characteristics such as shallower

anterior chambers, shorter axial lengths, and narrower angles compared to populations.

Hyperopia (farsightedness)

Hyperopic eyes are structurally smaller with shorter axial length and shallower anterior chambers. These features predispose to anterior chamber crowding and increase the likelihood of angle closure.

Female gender

Females are more commonly affected by PACG (10,13,17,18). This may be due to generally smaller ocular dimensions, including shallower anterior chambers and narrower angles, which increase susceptibility to angle closure.

Short axial length

A shorter axial length is associated with a smaller eye size and reduced anterior chamber depth. This anatomical configuration increases the risk of iridotrabecular contact and impaired aqueous outflow.

Thick and anteriorly positioned crystalline lens

A thicker lens or one positioned more anteriorly contributes to the narrowing of the anterior chamber angle. With aging, lens growth and forward displacement further exacerbate angle crowding.

Race and ethnicity

Variations in ocular anatomy among different racial and ethnic groups influence the prevalence of PACG. Populations with inherently shallower anterior chambers and narrower angles have a higher risk.

Family history of glaucoma

A family history increases the likelihood of developing PACG, suggesting a genetic predisposition. Familial aggregation indicates that inherited anatomical or physiological traits may contribute to disease (10,13,17,18).

Pathophysiology

According to the International Society for Geographical Epidemiological Ophthalmology (ISGEO), primary angle-closure glaucoma

(PACG) is defined as an eye with an occludable drainage angle and features indicating trabecular obstruction by the peripheral iris, together with evidence of glaucoma (1). This definition highlights the combined anatomical and functional components involved in the disease process.

The development of PACG is strongly influenced by structural ocular features. The main risk factors include a small cornea, a shallow anterior chamber, a thick crystalline lens, an anterior lens position, and a short axial length (10,13,17,18,19). These anatomical characteristics contribute to crowding of the anterior segment, predisposing the eye to narrowing and eventual closure of the anterior chamber angle.

Glaucoma, in general, refers to a group of progressive optic neuropathies characterized by excavation of the optic disc, apoptotic death of retinal ganglion cells, and progressive visual field loss (20). Retinal ganglion cells play a critical role in visual transmission, as their axons converge to form the optic nerve, carrying visual information from the retina to the brain. Damage to these cells leads to irreversible structural and functional impairment.

In PACG, angle closure impairs aqueous humor outflow through the trabecular meshwork, resulting in elevated intraocular pressure (IOP). Two primary mechanisms are responsible for angle closure: pupillary block and anterior displacement of the iris. In a pupillary block, resistance to aqueous flow between the posterior and anterior chambers at the level of the pupil causes pressure buildup in the posterior chamber. This pressure differential pushes the peripheral iris anteriorly, causing it to bow forward and contact the trabecular meshwork (iridotrabecular contact, ITC), thereby obstructing aqueous outflow.

In the 2nd mechanism, anterior displacement of the ciliary body, often related to its anatomical configuration or crowding, leads to

forward movement of the iris-lens diaphragm. This results in narrowing of the anterior chamber angle and subsequent iridotrabecular contact. Both mechanisms contribute to progressive angle closure and elevation of intraocular pressure (6).

Sustained elevation of intraocular pressure damages the optic nerve head, resulting in glaucomatous optic neuropathy. This is characterized by neuroretinal rim thinning, increased vertical cupping of optic disc (vertical cup-to-disc ratio >0.7), asymmetry in cupping (>0.2 between eyes), and corresponding visual field defects consistent with glaucoma (21). The pathophysiology of PACG involves a complex interplay between anatomical predisposition, impaired aqueous humor dynamics, and progressive optic nerve damage, culminating in irreversible vision loss if not detected and managed early.

Diagnostic approaches

The diagnosis of primary angle-closure glaucoma (PACG) is based on a combination of detailed history, clinical examination, and investigative techniques to identify anterior chamber angle closure, optic nerve damage, and functional visual loss. Early diagnosis is essential to prevent irreversible impairment.

History

Patients with primary angle-closure disease (PACD) should be evaluated for symptoms suggestive of intermittent angle-closure, including blurred vision, halos around lights, eye pain, headache, and ocular redness. These symptoms may occur spontaneously or be triggered by pharmacologic agents, including anticholinergics or mydriatic eye drops.

A thorough family history should be obtained, particularly regarding acute angle-closure crisis (AACC), as genetic predisposition plays a role in disease development. In addition, a detailed drug history is important, focusing on medications that may induce ciliary body

edema or precipitate angle closure, such as sulfonamides and adrenergic or anticholinergic agents (e.g., ipratropium bromide, salbutamol, and phenothiazines) (13,22).

The diagnosis of angle-closure glaucoma is based on the following criteria:

1. Closure of the anterior chamber angle (ACA), determined by indirect gonioscopy ($\geq 180^\circ$ non-visible posterior trabecular meshwork);
2. At least 1 clock hour of peripheral anterior synechiae and/or pigment deposition;
3. Intraocular pressure >21 mmHg on two separate occasions;
4. Presence of glaucomatous optic neuropathy (21, 23).

Clinical Examination

Slit-Lamp Examination

Slit-lamp biomicroscopy is used to evaluate the anterior segment, including anterior chamber depth, iris configuration, corneal clarity, and lens status. A shallow anterior chamber, mid-dilated pupil, or signs of prior angle closure may be observed.

Intraocular Pressure (IOP) Measurement

IOP measurement is an essential component of clinical evaluation in suspected glaucoma. Elevated IOP supports the diagnosis when correlated with structural and functional findings. It is measured using tonometry techniques as part of routine examination.

Anterior Chamber Angle Evaluation

Limbal Anterior Chamber Depth Measurement (LACDM)

The Van Herick method is a non-contact slit-lamp technique used to estimate anterior chamber depth by comparing peripheral anterior chamber depth with corneal thickness. It is graded into four categories (VHG 1–4) and is useful as a screening tool, although its accuracy in detecting angle closure varies (14, 25).

Gonioscopy

It is the gold standard for evaluating the anterior chamber angle. It allows visualization of angle structures and identification of iridotrabecular contact (ITC), as differentiation between appositional and synechial angle closure. Direct gonioscopy (Koeppe lens) is used in pediatric and surgical settings, whereas indirect gonioscopy with mirrored lenses such as Goldmann, Zeiss, Posner, Sussman, or Volk is commonly used in clinical practice. These lenses require a coupling medium and allow detailed assessment of the angle structures (14, 25).

Optic Nerve Head Evaluation

Fundoscopy examination is essential to assess glaucomatous damage. Findings include increased cup-to-disc ratio, neuroretinal rim thinning, notching, disc hemorrhages, and asymmetry between 2 eyes. Serial evaluation is important for monitoring progression.

Visual Field Testing (Perimetry)

Standard automated perimetry is used to detect visual loss. Common glaucomatous defects include nasal step, arcuate scotoma, paracentral scotoma, and generalized depression of the visual field. It is essential for staging and follow-up of disease progression.

Anterior Segment Imaging

Imaging modalities such as anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM) provide detailed visualization of the anterior chamber angle and associated structures. These tools assist in identifying angle closure, plateau iris configuration, and structural abnormalities not easily appreciated on gonioscopy.

Cornea Thickness

Central corneal thickness (CCT) is an important parameter in the evaluation of glaucoma, as it may influence the interpretation of intraocular pressure (IOP) measurements. Variations in corneal thickness can affect the

accuracy of tonometry, particularly Goldmann applanation tonometry. In the primary angle-closure glaucoma (PACG), central corneal thickness may show transient variations during episodes of elevated intraocular pressure. These fluctuations are thought to result from stromal and epithelial edema associated with acute or intermittent IOP spikes. However, long-term changes in corneal thickness are generally minimal and not significantly altered by the disease process.

Reported studies have shown that central corneal thickness remains relatively stable, with values around 525 μm at IOP levels of 20–40 mmHg and approximately 528 μm at IOP levels of 41–60 mmHg (26–28). Assessment of corneal thickness is therefore useful not only for understanding the biomechanical properties of the cornea but also for improving the interpretation of IOP readings and overall glaucoma evaluation.

Management

The goals in the management of primary angle-closure disease (PACD) are to reverse or prevent angle closure, control intraocular pressure (IOP), and preserve optic nerve function to prevent glaucomatous damage. Early detection and timely intervention are essential to minimize the risk of irreversible visual impairment. Management strategies are typically tailored to the stage of the disease, the severity of angle closure, and the presence of optic nerve damage.

In primary angle-closure suspects or early disease, prophylactic measures may be considered to prevent progression. Laser peripheral iridotomy (LPI) is commonly performed to eliminate pupillary block by creating an alternative pathway for aqueous humor flow between the posterior and anterior chambers. This helps reduce pressure differences across the iris and prevents anterior bowing of the iris.

Pharmacological therapy may be used to control intraocular pressure, particularly in acute or advanced cases. Medications such as topical beta-blockers, prostaglandin analogues, alpha-agonists, and carbonic anhydrase inhibitors are used to reduce aqueous humor production or enhance outflow. In acute angle-closure attacks, systemic medications may also be administered to rapidly lower IOP and alleviate symptoms.

In cases where laser treatment is insufficient or angle closure persists, surgical intervention may be required. Procedures such as lens extraction (especially when lens-induced mechanisms are significant), trabeculectomy, or glaucoma drainage devices may be indicated to achieve long-term IOP control. Lens extraction has gained importance in recent years, as removal of the crystalline lens can deepen the anterior chamber and widen the angle, thereby addressing the underlying anatomical cause of angle closure.

Dark room dynamic gonioscopy is useful for evaluating angle behavior under conditions that may provoke narrowing and for monitoring changes in anterior chamber angle configuration over time. Imaging modalities such as ultrasound biomicroscopy (UBM) and Anterior Segment Optical Coherence Tomography (AS-OCT) provides detailed visualization of anterior segment structures, helping to identify mechanisms of angle closure, assess plateau iris configuration, and guide management decisions (13). Overall, management of PACD requires a stepwise, individualized approach that combines medical therapy, laser procedures, and surgical interventions, with the primary objective of preventing optic nerve damage and preserving visual function.

This narrative review has several limitations that should be acknowledged. First, the literature search was restricted to English-language articles published between 2018 and

2025, which may have introduced selection bias and excluded relevant studies published in other languages or outside the specified time frame. Second, the use of selected databases such as PubMed, Scopus, Web of Science, Google Scholar, and ResearchGate may not have captured all available literature, potentially leading to incomplete coverage of the topic. Third, as a narrative review, this study did not include a systematic meta-analysis or quantitative synthesis of data, which limits the ability to provide pooled estimates or statistically compare findings across studies. Additionally, publication bias may have influenced the available evidence, as studies with positive or significant findings are more likely to be published than those with negative or inconclusive results.

Future perspectives

Future efforts in the management of primary angle-closure glaucoma (PACG) should focus on improving early detection through the implementation of effective screening programs, particularly in high-risk populations such as older adults, females, and individuals of Asian descent. Increasing public and awareness of the asymptomatic nature of early disease is essential to encourage timely ophthalmic evaluation and reduce delayed diagnosis.

Advancements in imaging technologies, including anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM), along with the potential integration of artificial intelligence (AI)-based diagnostic tools, may enhance early identification of individuals at risk and improve diagnostic accuracy. There is a need for large-scale, population-based, longitudinal studies to better understand the epidemiology, natural history, and progression of PACG across regions and ethnic groups. Such studies can contribute to the development of targeted prevention strategies and evidence-based

clinical guidelines to reduce the global burden of disease and associated visual morbidity.

Conclusion

Primary angle-closure glaucoma (PACG) remains a significant global cause of irreversible blindness, particularly in high-risk populations such as individuals of Asian descent, older adults, and females. Its often-asymptomatic progression in early stages contributes to delayed diagnosis and advanced presentation, making timely detection and intervention crucial. The disease is multifactorial in origin, involving a combination of anatomical predisposition, physiological mechanisms such as pupillary block and anterior iris displacement, and demographic and genetic risk factors. Advances in diagnostic modalities, including gonioscopy, anterior segment imaging, and optic nerve and visual field assessment, have improved the ability to detect and monitor the disease. Effective management requires a comprehensive and individualized approach, including medical therapy, laser procedures such as peripheral iridotomy, and surgical interventions. Early identification of at-risk individuals, along with appropriate screening and preventive strategies, plays a key role in reducing disease progression and associated visual morbidity.

In conclusion, increasing awareness, early diagnosis, and timely management are essential to reduce the global burden of PACG and prevent irreversible vision loss.

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