The ROYAL COLLEGE of OPHTHALMOLOGISTS

Clinical Guidelines

The Management Of Angle-Closure Glaucoma

Date of Evidence Search: December 2020
Date of Publication: XXXXXX
Date of Review: XXXXXX

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Contents

1. Introduction

1.1 Background

80 million people

Glaucoma is a leading cause of blindness affecting an estimated at 80 million people worldwide. It is an intermittently progressive optic neuropathy that results in visual field defects with a pattern that locates the pathological lesion in the pre-laminar optic nerve head. A reduction in intraocular pressure will slow or arrest progression of the disease in the vast majority of cases.

Glaucoma is traditionally divided into primary and secondary variants. The secondary form is a result of another ophthalmic or systemic disease which typically provokes a marked elevation of intraocular pressure. Common underlying conditions include neovascularization, uveitis or ocular trauma.

The primary variant of glaucoma occurs without evidence of a secondary precipitating disease. Primary glaucoma is classified according to the appearance of the iridocorneal angle. Aqueous fluid drains out of the eye via the trabecular meshwork, in the iridocorneal angle. Depending on whether the iris is, or is not, occluding the angle, two variants are termed primary angle-closure glaucoma (PACG) and primary open angle glaucoma (POAG) respectively.

POAG and PACG are fundamentally different in their clinical presentation and in their management pathways. PACG is a more pressure dependent disease than open-angle glaucoma. The treatment of PACG focuses on decompartmentalising the eye to break down barriers to circulation of aqueous flow inside the eye.

The natural history of PACG is typically divided into three stages. The first stage is termed suspected primary angle-closure and those affected are called primary angle-closure suspects (PACS). In this stage of the condition, there is contact between the iris and the trabecular meshwork but the intraocular pressure (IOP) is normal, there are no acquired adhesions between the iris and the corneoscleral coat (peripheral anterior synechiae – PAS). The optic nerve structure and visual function are normal.

Primary angle-closure (PAC) is the second stage in which the IOP has become elevated (either previously or currently), and/or there are peripheral anterior synechial scars that have developed between the iris and the trabecular meshwork. In this stage there is no evidence of glaucomatous damage to the optic nerve nor any visual field abnormality.

The third and final stage is the development of primary angle-closure glaucoma (PACG). It is possible for patients to develop PACG without elevated IOP having been detected and also in the absence of PAS.

The florid, symptomatic presentation of angle-closure, called acute angle-closure (AAC), is the result of sudden, total occlusion of the trabecular meshwork which causes extreme ocular hypertension. Symptoms of pain, sudden reduction (or even loss) of vision, nausea and/or vomiting can be profound and dramatic. Previously, AAC was regarded as a “rapidly blinding” condition. With prompt presentation and appropriate management, this condition is not as feared as it once was.

PACG causes a higher rate of severe visual loss than does POAG. Although POAG affects approximately three times as many people globally as does PACG (60 million versus 20 million), the numbers of people blinded by POAG and PACG are roughly equal. This greater propensity to cause serious loss of vision makes clinicians justifiably cautious in managing PACG and has prompted many to consider preventive treatment.

1.2 Population to whom the Guideline applies

Angle-closure glaucoma typically affects elderly patients. PACG is rare among adults under the age of 40 and, when it does occur, is thought to be predominantly the result of a plateau iris mechanism. The disease is very rare but has been documented in children. Angle-closure occurs with approximately a 3:1 female to male ratio. Racial heritage is a widely recognised risk factor for angle-closure disease. Asian people suffer a higher burden of angle-closure, with a three-fold greater incidence of acute angle-closure in Chinese patients compared to Caucasians. Angle-closure glaucoma is uncommon among Africans.

ICD10 Codes	
H40.03	Anatomically narrow angle (PACS)
H40.06	Primary angle-closure without glaucoma (PAC)
H40.2	PACG
H40.20	Unspecified PACG
H40.21	Acute angle-closure glaucoma attack/ crisis
H40.22	Chronic angle-closure glaucoma
H40.23	Intermittent angle-closure glaucoma
H40.24	Residual stages of angle-closure glaucoma
H40.6	Glaucoma Secondary to drugs (especially T43.3X5(ADS) psychotropic drugs)
H40.83	Aqueous misdirection
H21.82	Plateau iris syndrome (post iridectomy)
T49.5X5	Adverse effects of ophthalmological drugs and preparations

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1.3 Current practice, and why there is scope for change

In September 1857, Albrecht von Graefe reported the use of surgical iridectomy in the management of glaucoma. Surgical iridectomy has since been a cornerstone of management of angle-closure glaucoma until the mid 1970's when it was superseded by laser peripheral iridotomy (LPI). LPI has been widely used as a treatment but also increasingly deployed as a preventative strategy. The role of preventive LPI in the fellow eye of someone who has suffered an acute angle-closure crisis is unquestioned.

The publication of the results of the EAGLE trial in 2016, has provided new evidence to guide the management of PAC and PACG. This trial randomised patients with either PAC with IOP above 30 mmHg, or with PACG, to receive either LPI or clear lens phacoemulsification. EAGLE represents probably the most significant advance in the management of angle-closure glaucoma since the invention of the surgical iridectomy. It is now clear that lens extraction is generally safe, highly effective, cost-effective and benefits patient's quality of life compared to LPI in patients meeting enrolment criteria. This has led to a profound shift in management away from the use of LPI in PAC and PACG.

The use of LPI as a preventative treatment in people who are asymptomatic and have never had a documented pressure rise is widely practiced but has no firm evidence base. Around

75% of all UK ophthalmology consultants offer a prophylactic LPI to patients with narrow or occluded drainage angles.

The events of the first six months of 2020 have brought the NHS under unprecedented pressure, and is prompting a fundamental re-examination of the justification for previously entrenched patterns of practice.

In the year 2018-19, NHS hospital statistics for England recorded 13,844 patient episodes with a primary procedure identified as LPI. The majority of these will have related to prophylactic procedures. This represents significant capacity burden and, therefore, the role of LPI needs to be very carefully scrutinised.

2. Objectives

2.1 Main Aims

The scope of this guideline covers the primary angle-closure spectrum only and specifically excludes secondary disease such as that resulting from uveitis or neovascularization.

This guideline has been written primarily for clinicians involved in eye care in the community and in hospital eye services and aims to inform clinicians on 4 main points

1. What is the accuracy of current diagnostic tests
2. What is the effectiveness of different interventions
3. When to refer to hospital eye services
4. When to discharge to community

2.2 Key Clinical questions

Epidemiology

a. What is the Primary Angle Closure spectrum of disease and how should patients be classified?
b. What is the prevalence in the UK (or Europe/White US if minimal data exists for the UK)
c. What is the visual morbidity (including notifiable sight impairment) caused by PACG in the UK (or Europe/White US if there is minimal data for the UK)?
d. What are the known risk factors for PACG?
e. What is the natural history of untreated and treated disease?

Diagnosis

f. What is/are the optimal and/or acceptable test(s) for diagnosis (secondary/tertiary)
g. Should provocative tests be used?
h. What is the optimal and/or acceptable test(s) for case detection (optom/primary care)

Management of primary angle-closure disease?

i. When to do a prophylactic laser iridotomy
j. Laser iridotomy as prophylaxis in the fellow eye of people suffering acute angle-closure
k. What is the optimal and/or acceptable management of an acute angle-closure crisis
l. What is the optimal and/or acceptable management of primary angle-closure with glaucoma
m. What systematic reviews and meta-analyses exist that can guide management?
n. What are the appropriate laser, medical and surgical interventions in established disease?
o. Is there evidence that management should differ in different racial groups (For instance, should Asian or African people be offered different management)?

Patient Follow up

p. How to manage residual iridotrabecular contact (ITC)

q. Management of cataract in angle-closure (whether to perform LPI before phaco?)

r. How to handle pupil dilation in suspected or established angle-closure

3. Methods

3.1 Search strategy

Key questions for the guideline were developed using the PICO framework to provide a structured basis for identifying the evidence. A systematic review of the literature was undertaken using the explicit search strategies devised in collaboration with the Cochrane Eyes and Vision Group. Databases searched include Medline, Embase, and the Cochrane Library for literature published between 2000 & 2017. Further searches were undertaken on various websites including the US National Guidelines Clearinghouse.

The evidence base for this guideline was identified and synthesized in accordance with the accepted methodology. Each of the selected papers was evaluated by the guideline development group using standard checklists before conclusions were considered as acceptable evidence. The literature search focused on the best available evidence to address the key review questions by including the following types of evidence

- Published guidelines
- Systematic reviews
- Randomised controlled trials
- Cohort and case control studies
- Case series

Papers not published in the English language, conference abstracts and letters were excluded.

3.2 Evidence and grading

We graded the quality of evidence and the strength of recommendations in line with the system published by the GRADE Working Group[1]:

Levels of evidence

- **High** = Further research is very unlikely to change our confidence in the estimate of effect (e.g., large, well conducted, definite RCTs)
- **Moderate** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate (e.g., small or potentially biased RCTs, non-randomised comparative studies)
- **Low** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate (e.g., observational studies)
- **Very low** = Any estimate of effect is very uncertain.

4. Recommendation for Practice

- **Strong: "Do it" or "don't do it"** – indicating a judgment that most well-informed people would make; (e.g., large, well conducted, definite RCTs)
- **Weak: "Probably do it" or "probably don't do it"** – indicating a judgment that a majority of well informed people would make but a substantial minority would not.

4.1 Terminology & Disease Definitions

Primary angle-closure is defined by contact between the iris and trabecular meshwork in the absence of other ocular or systemic diseases (e.g. uveitis or neovascularization). Primary irido-trabecular contact (ITC) is therefore the hallmark of the disease, which may sometimes lead to secondary elevation of intraocular pressure (IOP). This may in turn cause sight loss as a result of glaucoma, or sometimes through other diseases such as cataract or retinal vascular disease. Glaucoma denotes damage to the retinal ganglion cell axons at the level of the pre-laminar optic nerve head causing reproducible visual field loss. Glaucoma is slowed or arrested by reduction of intraocular pressure. Primary angle-closure glaucoma, therefore, indicates loss of visual function and structural damage to the optic nerve occurring in the setting of an occluded drainage angle, with an assumed underlying mechanism mediated by elevated intraocular pressure. As with all forms of glaucoma, other explanations for loss of vision should be considered and if necessary, excluded by further investigation.

The acute presentation of angle-closure is a well-known ophthalmic emergency. This sudden, profound ocular hypertension causes dramatic symptoms. Both the disease and the ensuing medical treatment can make patients seriously ill. Acute symptoms are associated with presentation earlier in the natural history of angle-closure disease than those without symptoms [2]. However, the longer-term prognosis for these people is that 9% become blind from glaucoma, and a similar proportion have been reported to suffer sight loss from unoperated cataract [3].

Research has identified weaknesses in the traditional classification of angle-closure disease which focusses on the presence or absence of symptoms, identifying acute, subacute and chronic forms of angle-closure. While symptoms of blurring, haloes and pain in and around the eyes are relatively common in people with angle-closure, they also occur in a large proportion of the "normal" population [4]. In addition, the term "narrow angle" or "narrow angle glaucoma" has also been used to describe this condition in the past. This is unhelpful, as the disease of angle-closure only occurs in people where iridotrabecular contact is present. By including people with narrow but open angles in the group requiring medical attention, many people who have no significant risk of vision loss from angle-closure disease will undergo treatment, or absorb monitoring resources during follow-up. It is therefore recommended that classification is based on physical signs relevant to the current visual function, or the prognosis of future visual loss. An important gap in current evidence is the relevance of peripheral anterior synechiae (PAS) to visual prognosis of people who suffer angle-closure. There are two classification frameworks that help inform and guide clinical modern management. These are natural history staging of the disease, and an assessment of the likely underlying mechanism responsible for the angle-closure.

Natural History Staging of Angle-closure Disease [5]

a. Primary angle closure suspect – this is defined by iridotrabecular contact in the presence of normal intraocular pressure and no evidence of glaucomatous optic neuropathy.

b. Primary angle closure – In this second stage, intraocular pressure is elevated. There is no evidence of glaucomatous optic neuropathy. Other forms of ocular pathology, such as lens opacities or retinal vascular disease, may be present.

c. Acute angle closure (AAC) crisis – The physical signs that follow the dramatic symptoms of an acute angle closure crisis do not always have an impact on the long-term visual prognosis of patients, but they are relevant because of the potential (often reversible) impact on current visual function. Symptoms are typically attributable to lens opacities or a dilated, unresponsive pupil resulting from iris ischemia. Glaucomatous optic neuropathy may be seen in the setting of an acute symptomatic presentation. It is likely this was a pre-existing phenomenon and not the result of an acute pressure rise spanning a matter of hours or days. In AAC, there is a need for expeditious management which differs from routine care, which makes the acute crisis an important variant in disease natural history.

d. Primary angle closure glaucoma – In the final stage, glaucomatous optic neuropathy has developed in the setting of an occluded drainage angle. Glaucoma is defined by structural abnormalities in the pre-laminar optic nerve head, together with reproducible visual field loss.

Underlying mechanism of angle closure

The conceptual framework identifying the location of obstruction to circulation of aqueous within the eye helps clinicians create individually targeted management plans appropriately. A widely used classification identifies four potential levels of obstruction each progressively more posterior.

a. Obstruction at the level of the pupil (i.e. pupil-block)

b. At the level of the ciliary body (i.e. plateau iris and/or peripheral iris crowding)

c. At the level of the lens or resulting from lens intumescence (lens induced angle-closure)

d. Behind the lens, within the vitreous or the retina

However, in terms or management the key distinction is to differentiate anterior (a & b) from posterior (c & d)

Practice point
Most cases of angle-closure are primarily the result of pupil block (75%), and as such, iridotomy may be effective at controlling earlier stages of disease. However, pupil block and plateau iris mechanisms may co-exist, and hence, it is important to consider performing a laser iridotomy even if a non-pupil-block mechanism is suspected. Although the lens plays an important role in the pupil block mechanism, the term ‘lens-induced glaucoma’ is best reserved for cases with a white, intumescent or unstable lens. Lenticular and retro-lenticular block are uncommon, accounting for approximately 5% and 1% of angle-closure presentations in the UK respectively. However, they are very important to recognize in acute presentations as, in contrast to pupil block and anterior non-pupil-block mechanisms (which respond well to treatment with pilocarpine in the initial stages), lenticular or retro-lenticular block are typically aggravated by pilocarpine treatment. Cycloplegia with cyclopentolate or atropine are the effective initial medical treatments in these less-common cases.

4.2 Epidemiology

d. What is the prevalence in the UK (or Europe/White US if minimal data for UK)

A systematic review concluded that it affects 0.4% of the white, European adults aged over 40, amounting to 130,000 in the UK and 1.6 million people throughout Europe. Projected changes in demographics suggest that prevalence may increase by 20% per decade, because of greater life expectancy. [6]
This implies that, while not the most common form of glaucoma (prevalence of primary open angle glaucoma in Europe is around 2.5%), [7] PACG is not a rare condition, and may account for approximately one case in 6 of glaucoma in the UK.

b. What is the visual morbidity (including notifiable sight impairment) caused by PACG in the UK (or Europe/White US if minimal data for UK)?

Data on the visual morbidity from PACG in white Europeans is very limited, and not of high quality. A review of data from prevalence studies worldwide projected that, in 2020, PACG has caused bilateral severe visual impairment in 5.3 million people, compared with 5.9 million people blinded globally by primary open angle glaucoma. [8]

c. What are the known risk factors for PACG?

A shallow central and peripheral anterior chamber has consistently been identified as a risk factor for primary angle-closure disease, [9] primary angle-closure glaucoma, and acute angle-closure crises. [10]

Other clinical characteristics are widely thought to be associated but are less well proven. A shorter axial length, and thicker, more anteriorly positioned lenses are plausible risk factors. [11] While there is a relationship between hypermetropic refraction and angle-closure disease, it is important to recognise that this is not consistent and that cases of angle-closure do occur in people with a myopic refraction. Therefore, refractive error should not be used to determine which patients are assessed for risk of angle-closure.

Occluded drainage angles are heritable phenomenon. [12] Genome-wide association studies (GWAS) have identified a range of single nucleotide polymorphisms that are linked to increased angle-closure risk. [13] [14]
Of note, COL11A1 (the gene in which mutations cause Stickler's syndrome) has been identified as increasing the risk of angle-closure disease. The frequency of overt secondary angle-closure in conditions such as Marfan/Weill Marchesani syndrome, and Ehler-Danlos syndrome, further underlines the association between angle-closure disease and abnormal ocular connective tissues. Retinitis Pigmentosa is associated with angle-closure. [15] Similarly, Best Vitelliform Macular Dystrophy is associated with angle-closure disease. [16]
Recently, mutations in the gene SPATA13 have been linked to familial cases of angle-closure in white UK citizens, constituting the first causative gene for angle-closure. [17]

It is therefore important that, whenever a new case of angle-closure glaucoma or acute angle-closure is identified, family members are made aware that they should observe NHS sight-testing guidelines. Referral of first-degree relatives is advised if a potentially occluded drainage angle is identified in this testing.

Practice point

First degree relatives of patients who are diagnosed with significant primary angle-closure disease (i.e not primary angle-closure suspects) should be advised to undergo regular community optometric reviews, and then referred to hospital eye services for consideration of prophylactic laser iridotomy, if they meet current referral criteria.

Research need

Strategies for identification of occluded drainage angles in first degree relatives should be evaluated. This research may compare community optometric case-finding with direct referral to the hospital eye service.

Summary of evidence:

- Shallower anterior chamber depth is a risk factor for PACG
- Occluded angles and angle-closure disease are heritable

d. What is the natural history of untreated and treated disease?

Studies of incident (newly occurring cases) acute angle-closure crises give insights into the rates of angle-closure in different ethnic and racial groups in the global population. The rates are typically expressed as number of cases occurring per year in 100,000 people, and usually address the population aged 30 years and older. Reported rates of between 2 – 5 /100,000/year in European populations. [18 19] In Chinese populations, the incidence rate ranges between 12 – 16/100,000/year. [20 21] Rates among the South and Southeast Asian people are intermediate at 6 – 7 /100,000/year. [21 22] These studies typically use hospital episode data to identify cases, and consequently are subject to some bias.

A recent trial of prophylactic laser iridotomy, which enrolled people with occluded drainage angles (PACS) in a large urban centre in the People's Republic of China, quantified the risk of incident angle-closure disease in untreated eyes of trial participants. The headline risk was of 8 new cases/1,000 years (36/889 eyes over 6 years follow-up). By far the most common clinical manifestation of disease was of new peripheral anterior synechiae (PAS, 30/889 eyes). Elevated intraocular pressure was uncommon (5/889 eyes) as were acute angle closure crises (5/889 eyes). Three eyes reached simultaneous IOP and PAS end-points. There were no cases of incident glaucomatous optic neuropathy over the six-year follow-up period. [23] The implications of these findings are that, in people with occluded drainage angles (PACS), progression of angle-closure disease is uncommon, even in the highest risk population on Earth. Consequently, the risks of significant loss of vision are similarly small over this timescale.

A cautious interpretation of the data would be that the UK population are at the same risk as the population in China. Informing patients with narrow or occluded drainage angles that the risk of an acute angle-closure crisis is around 1/1000 per year would be a simple, easily remembered figure. In light of the incidence data, a more accurate interpretation would be that the true risk will be lower by a factor of 3 or 4 for the white UK population.

Summary of evidence:

- The risk of incident sight-threatening angle-closure disease (symptomatic or asymptomatic) in people with occluded drainage angles (PACS) and no other abnormality or risk factor is less than 1/1000 per year **(Evidence/recommendation: High; Strong)**

4.3 Diagnosis

s. What are the recommended tests for diagnosis in secondary and tertiary care

Gonioscopy remains the cardinal technique for diagnosis and monitoring of primary angle-closure disease. The ability to perform dynamic gonioscopy provides clinicians with unique insights into anterior segment drainage angle anatomy that is not possible with other examination techniques. However, gonioscopy is an unpleasant examination for some patients. It is also technically exacting and requires practice and training to perform the examination competently. More difficult examinations, especially in those with established angle-closure disease, can be time consuming. In the UK, pressure on NHS outpatient clinics means that alternative investigations are vital to maintain efficient delivery of care.

The assessment of limbal anterior chamber depth (LACD or the "van Herick" test) remains a useful quick assessment which should be carried out in addition to gonioscopy. [24] This test is easier for paramedical support staff and optometric professionals to both learn and to perform in primary and secondary care settings. The fact that this is a non-contact examination is a great advantage.

The advent of anterior segment imaging techniques such as high frequency ultrasound biomicroscopy and anterior segment OCT (AS OCT) provide sophisticated additional methods of assessment of the anterior segment anatomy. These may be used to generate numeric data which may prove useful in assessing future risk of disease. AS OCT is particularly useful because it offers a quick, non-contact method of creating a documentary record of angle anatomy which can be reviewed remotely in virtual clinics, and used for audit. AS OCT can be performed in lower light conditions that may reveal unrecognised angle-closure disease.

AS OCT can identify irido-trabecular contact (ITC), but this role may be limited by problems with identification of key landmark – the scleral spur or Schwalbe's line. Research shows that that AS OCT typically identifies more ITC than gonioscopy. [25] Angle anatomy is inherently variable but some studies suggest that limbal chamber depth assessment and AS OCT give more consistent assessments than gonioscopy for detecting people at risk of angle-closure. The significance of this observation is unproven, but it is reassuring if these tests are used in technician led virtual clinics. AS OCT can objectively document pre- versus post-PI treatment differences in angle width which will help clinicians understand the impact of treatment, and can be of great help in demonstrating the problem and confirming the outcome of treatment with patients. Despite these attractive features, the utility of anterior segment imaging or biometry has never been proven to have any utility to identify which patients will suffer glaucoma in the future.

A recent Cochrane review found sub-optimal quality of evidence regarding the diagnostic performance of LACD and AS-OCT. Pooled data showed that LACD had high sensitivity and a sufficient specificity for case-finding and performed as well as more sophisticated imaging equipment. However, the authors highlighted that "There is still a need for high-quality studies to evaluate the performance of non-invasive tests for angle assessment." [26]

Practice point

Gonioscopy remains the definitive examination for diagnosis and monitoring of angle-closure disease. Anterior segment OCT (AS OCT) is an important supplementary test, but cannot replace gonioscopy for detection of PAS. As has been noted above, the relevance of PAS to visual prognosis is currently unclear.

Research need
Longitudinal studies are needed to validate the diagnostic and prognostic significance of AS OCT parameters for identifying individuals at risk for PAC and to predict disease progression and effectiveness of interventions. The relevance of PAS to the visual prognosis of patients is unproven.

Summary of evidence:

- We SHOULD continue to use gonioscopy for diagnosis
- AS-OCT is a useful supplement to gonioscopy, producing a documentary record, and may streamline follow-up especially around pre- & post- treatment but cannot replace gonioscopy for diagnosis.
- In secondary care, AS-OCT may be used as a triage test, to exclude the need for gonioscopy as part of referral refinement.

t. Should provocative tests be used?

The known relationship between pharmacological dilation of the pupils and the onset of symptomatic ocular hypertension in angle-closure [19] suggests that diagnostic/therapeutic pupil dilatation may have a role in identifying people at particular risk of angle-closure disease.

The fact that pharmacological dilation of the pupils is a non-physiological activity has prompted the examination of other stimuli as potential tools to identify those at increased risk. These include the face down test and the darkroom test and the combination of these two. In a refinement to pharmacological testing, the co-application of pilocarpine and phenylephrine drops seeks to splints the pupil in a mid-dilated position, which is thought to be the position which creates the greatest risk of a significant pressure rise in angle-closure disease.

Provocative tests have had a controversial history with some experts regarding them as “time-consuming, potentially misleading and possibly dangerous”. There is no evidence that they consistently identify people at significant risk of angle-closure disease. The best randomised controlled trial carried out as a nested study within the ZAP study showed that a short dark prone provocative test did not help to identify people who reached an endpoint within the trial. [27] Therefore, the use of provocative tests is not currently recommended.

- There is no evidence to support the use of provocative tests for diagnosis or monitoring in PAC/PACG **(Evidence/recommendation: High; Strong)**

u. What are the recommended tests for case detection in community and primary care

To date, the Hospital Eye Service has accepted referrals from community optometrists and primary care practitioners when it is believed that angle-closure is possible. These people would represent primary angle-closure suspects (PACS). By definition, if they were referred on the basis of an occludable drainage angle alone, their intraocular pressure, optic disc anatomy and visual field status would be normal.

Tests used in community optometry and primary care settings would necessarily be technically straightforward to perform, relatively quick and cost neutral. However, the growing availability of OCT machines in community optometry practice brings a technically sophisticated but user-friendly technique into play as a potential case detection tool.

A recent Cochrane review has assessed the non-contact methods available to detect people at risk of primary angle-closure glaucoma. Five non-invasive tests were studied. These comprised the oblique flashlight test, LACD, AS-OCT, Scheimpflug photography and scanning peripheral anterior chamber depth analyser (SPAC), all of which either measure or estimate the dimensions of the drainage angle. The conclusion was that, although the quality of studies was sub-optimal, limbal anterior chamber depth, a quick and simple test, has high sensitivity and specificity to diagnose angle-closure. The authors did comment that the test could be useful for targeted screening in populations with a high prevalence of the condition. [26]

AS OCT, when available, is a very useful supplement. It creates a documentary record of the examination finding which may be sent to the secondary/tertiary care practitioner for triage purposes.

In light of the evidence identifying a low risk of sight loss from glaucoma or pathology related to acute angle-closure in people with occluded drainage angles, it is now advised that referrals be made in line with NICE guidance for raised IOP or glaucoma. Those with presumed occluded angles should only be referred on the basis of elevated IOP, glaucoma, or the following risk factors constituting "PACS PLUS".

"PACS PLUS"

Criteria for Referral of People with Suspected Occluded Angles to the Hospital Eye Service

Angle Criteria

Either – a limbal chamber depth grade < ¼

Or – an anterior segment OCT showing irido-trabecular contact (ITC)

PLUS: one of the following criteria

- People with only one "good eye" in which deterioration of vision may threaten independent living or livelihood
- Vulnerable adults who may not report ocular or vision symptoms
- Family history of significant angle closure disease
- High hypermetropia (> + 6.00 dioptres)
- Diabetes or another condition necessitating regular pupil dilation
- Those using antidepressants or medication with an anticholinergic action
- People either living in remote locations (such as foreign aid workers, armed forces stationed overseas or oil rig workers etc.) where rapid access to emergency ophthalmic care is not possible

The finding of "PACS PLUS" should trigger referral to the Hospital Eye Service

"PACS MINUS"

If an individual has the angle-characteristics specified above but none of the "plus" criteria, and does not meet NICE glaucoma referral guidelines, they should be advised to seek an annual NHS sight test.

4.4 Management

v. What is the recommended management of primary angle-closure disease

The major advance in evidence informing the management of primary angle-closure disease comes from the 2016 EAGLE randomised control trial (RCT) which enrolled patients with either primary angle-closure glaucoma (regardless of IOP) or primary angle-closure disease with a IOP >/= 30 mmHg and randomised these participants to receive either clear lens phacoemulsification or laser iridotomy. This trial showed that clear lens phacoemulsification was superior to laser iridotomy in terms of metrics of disease control, the economic measures and patient reported outcomes. Clear lens phaco was resulted in better IOP control to laser iridotomy. After 3 years, IOP was 1 mmHg lower in the phaco group but with less medications (the rates of being off medication were 60% versus 20% in the two groups) and less number of glaucoma surgeries (0.5% vs 11% in the phaco and laser PI group, respectively). Phaco was cost-effective, showing cost savings in economic modelling. Quality of life remained stable in the phaco group, but dropped in the LPI group. [28] The question of whether goniosynechiolysis (GSL) provides any supplementary benefit to phacoemulsification alone has been addressed in some RCTs which showed no benefit to the additional use of the GSL. [29 30]

Effectiveness of LPI may decrease with greater severity of the disease. Studies showed that most PACS eyes did not need any further intervention after LPI, while many PAC, PACG, and acute PAC eyes required additional treatment to control IOP. The question of whether laser iridotomy location has any bearing on the troubling side effect of dysphotopsia has been examined in three clinical trials which showed opposing results. A small RCT carried out in Canada suggested that a temporal location of iridotomy reduced rates of dysphotopsia symptoms [31] while a larger study in India showed that no effect of laser iridotomy site on the rate of dysphotopsia symptoms. [32] There appears to be no difference in rate of bleeding with discontinuation of anticoagulant treatment providing INR levels remain below 3.0. [33]

Laser peripheral iridoplasty has been proposed for eyes with remaining appositional angle closure after LPI. Two RCT's identified no benefit for IOP control for laser iridoplasty when used in addition to laser iridotomy in PAC/PACG. [34 35]

Summary of evidence:

- Phacoemulsification lens extraction is preferred over laser PI for PAC disease with IOP > 30mmHg **(Evidence/recommendation: High; Strong)**
- Goniosynechialysis has been shown to have no benefit and therefore should not be carried out **(Evidence/recommendation: Moderate; Weak)**
- There is no need to stop anti-coagulants for PI when INR < 3 **(Evidence/recommendation: Moderate; Weak)**
- Studies have shown no consistent evidence for PI location influencing dysphotopsia: PI may be placed at either superior (12 o'clock) or temporal locations **(Evidence/recommendation: Moderate; Weak)**
- Residual ITC is common after PI (seen in 20-80% of cases). No evidence supports further interventions for ITC alone. It may be used to risk-stratify follow-up after PI. **(Evidence/recommendation: Moderate; Weak)**
- Laser peripheral iridoplasty has been shown to have no IOP lowering benefit. **(Evidence/recommendation: High; Strong)**

w. When to do a laser iridotomy in narrow angles/occludable angles/PACS

In a large RCT of screening for PACG carried out in Mongolia (N= 4,725), the population was enrolled and underwent randomisation to either no intervention or to screening with measurement of central anterior chamber depth. If screened participants met criteria for PACS, these people were offered laser iridotomy. At the end of the study, incident glaucoma rates were compared between the intervention (screened) and the untreated control group. This study showed that there was no difference in the rate of new glaucoma between the control group and the screened group. In this context, the trial concluded that there was no benefit for population-wide screening and prophylaxis for people at high risk of PACG. [36]

The ZAP study, carried out in southern China, enrolled 11,991 people over the age of 50, and identified 889 with PACS. These people were randomised to receive laser iridotomy in one eye and no treatment in the other eye. Iridotomy halved the risk of new angle-closure disease (HR 0.53 over 6 years), i.e., raised IOP and/or new PAS, but the rate of new disease in both treated and untreated eyes was very low (4.2 versus 8.0 cases of PACD per 1,000 eye years). Most cases were identified on the basis of new PAS, which appeared to pose little immediate risk to loss of vision. The number needed to treat (NNT) to prevent PAC (PAS, raised IOP, or very rare acute crises) was 44 over 6 years. There were no cases of incident glaucoma identified in this trial in treated or untreated eyes, and no cases of severe visual impairment. Using the best available data to extrapolate the NNT to prevent glaucoma, a projected figure of 126 to prevent one case of glaucoma over 10 years. [23] As the older Chinese population appears to be one of the highest risk groups globally for PACG, it is reasonable to assume that the risk to the UK population (with much lower prevalence and incidence of PACD) is no higher than that seen in ZAP. Whether the same results are applicable to non-Chinese populations remains to be proven.

As preventive treatment was of minimal benefit numerically in the high-risk Chinese population, the most logical conclusion here is that there is no benefit from large-scale prophylactic laser iridotomy treatments in the UK. An economic analysis which attempts to extrapolate the ZAP data to the UK NHS situation is underway, and will provide an additional perspective on the case for prophylaxis. A sister study of ZAP, carried out in Singapore (ANALIS), is similarly underway and likely to report results soon. Preliminary reports from ANALIS point to similar outcome as seen in ZAP. On the basis of the medical data available currently, routinely offering prophylactic treatment to all people classed as PACS is not currently advised. Laser PI may be advisable for people with high-risk PACs (see below)

Heritability studies and molecular genetic studies outlined above suggest that PACD will cluster in families. A natural assumption is that family members of those with PACD or PACG are at inherently higher risk than other members of the population. However, this specific question has never been addressed. People who require regular pharmacological dilation of the pupils for monitoring of retinal disease are at increased risk of acute angle-closure crises. [19]

Research need

- It is currently unclear if the finding of PAS indicates a significant risk of sight loss. An observational study of the natural history of eyes with PAS is needed to determine if these people should be monitored, or even identified.
- It is unknown if people who have a family history of PACD or who harbour a known genetic risk variant are at higher risk of developing glaucoma (i.e. loss of vision) than the general population. With the increasing availability of genetic testing, and the rise of “precision medicine”, understanding the implications of heritable risk will be increasingly important.

Summary of evidence

- There is no benefit in screening for (i.e. in attempting to detect precursors of, and prevention of,) PACG in a high risk Asian populations **(Evidence/recommendation: High; Strong)**
- Although a high-quality trial has shown laser PI reduces (halves) the risk of incident PAC disease in high risk population (Chinese over the age of 50 years with PACS), the risk of incident disease is small. Thus, most people are likely to receive little benefit from prophylactic PI. **(Evidence/recommendation: High; Strong)**
- Until further evidence is forthcoming, laser PI **IS** advised for people with PACS **PLUS** additional risk factor(s) such as an "only eye", a family history of significant angle closure disease, high hypermetropia, diabetes or another condition necessitating regular pupil dilation, use of antidepressants or medication with an anticholinergic action, and those people either living or working in remote locations (such as foreign aid workers, armed forces stationed overseas or oil rig workers) where accessing emergency ophthalmic care is not possible. **(Evidence/recommendation: Low; Strong)**
- Laser PI **IS NOT** advised for most people with PACS with no additional risk factors. **(Evidence/recommendation: High; Strong)**

x. Laser iridotomy in the fellow eye of people suffering acute angle-closure

Contralateral fellow eyes of those which have suffered an acute attack are at high risk of suffering a similar fate.[37 38] Laser iridotomy appears effective in preventing long term IOP rises in around 90% of these eyes. [39] Although never subjected to an RCT, laser iridotomy is viewed as mandatory in the fellow eye of those who have suffered and acute angle-closure crisis. [40]

Practice point

Anecdotally, ophthalmologists have encountered patients who have re-presented within days with acute crises in their fellow eye when discharged without undergoing a laser iridotomy. It is therefore strongly advised that laser iridotomy be attempted in the fellow eye without delay, before the patient is discharged, once their IOP is controlled.

- Laser iridotomy **IS** recommended for all contralateral eyes when acute (symptomatic) angle-closure has occurred in the fellow eye. This should be done at the time when the acute angle-closure is treated. **(Evidence/recommendation: Low; Strong)**

y. What is the recommended management of an acute angle-closure crisis

The acute management of an angle-closure crisis has been the subject of remarkably few randomised controlled trials and therefore robust data on management is relatively sparse. However, the principles for managing this relatively common ophthalmic emergency are not controversial.

Most patients will be in moderate to severe pain with acutely reduced vision. Nausea and vomiting are relatively common. Therefore, the immediate priorities are analgesia, antiemesis and rapid confirmation of diagnosis, with subsequent topical and systemic medication to reduce the intraocular pressure.

The most important management decision must be confirming that angle-closure is present, and that intraocular pressure is elevated. Once this has been established, it is crucial to exclude secondary causes of angle-closure. If lens-induced or retro-lenticular mechanisms of angle-closure are not recognised and

treated appropriately with cycloplegia (i.e. atropine or cyclopentolate), the use of topical pilocarpine will aggravate the condition and result in prolonged pain and a delay in controlling intraocular pressure.

The key physical sign and that will help to quickly identify and a lenticular or retrolenticular secondary mechanism is a marked asymmetry of the central anterior chamber depth. The only regularly-reported scenario in which a bilateral presentation of angle-closure attributable to posteriorly segment mechanisms is that associated with the use of topiramate causing supraciliary effusions and anterior rotation of the ciliary body. [41] Therefore, use of topiramate should be routinely sought on direct questioning in suspected cases of atypical angle-closure.

In acute angle-closure, regardless of whether this is thought to be pupillary block or non-pupil-block plateau iris, after the cardinal intervention is laser peripheral iridotomy, which should be done as quickly as possible. The use of intensive pilocarpine drops is not advised. After an initial instillation of pilocarpine an appropriate dosage frequency would be every six hours. Probably the single most useful medical agent that should be employed in the initial stages of pressure control is systemic acetazolamide. As there are potentially serious drug allergies or side-effects, it should quickly be established the patient has no history of allergies to sulphonamide medications such trimethoprim, and no severe nephropathy. Other topical ocular antihypertensives should be used as the situation and medical history indicate. Intensive initial anti-inflammatory treatment with topical steroids is recommended.

Acute Angle Closure Care Pathway (pupillary block or plateau iris mechanism)

Analgesia and anti-emesis if required

Examination to exclude to confirm elevated pressure from angle-closure, and to identify/exclude secondary causes, lenticular and retro-lenticular causes

Identify any prior allergies/contraindications

Stat medication
G. Dorzolamide 2%/G. Timolol 0.5% combination
G. Apraclonidine 0.5%
G. Pilocarpine 2%* (defer if IOP> 40 mmHg)
IV Acetazolamide 250mg (if IOP> 40mmHg)

Review after 30-60 minutes

If laser iridotomy technically feasible (cornea clear, patient comfortable), proceed to laser peripheral iridotomy in both eyes

When PI complete, commence G. Dexamethasone 0.1% or G. Prednisolone 1% at minimum of hourly while awake for 24 hours then 4 x day for one week

If no/insufficient response by 2 hours, or technically not possible to do (cornea oedematous) consider laser peripheral iridoplasty or diode laser cycloablation (recommend all NHS Eye Depts with urgent care service have diode)

Secondary cases should receive care directed at primary pathology (e.g. drug-induced uveal effusions such as topiramate, neovascular and uveitic)
* Atropine 1% is substituted for pilocarpine if lenticular/retro-lenticular causes

Practice point
An important safety point when deciding on treatment regimen would be to enquire about the presence of coronary artery disease causing angina, prior myocardial infarction or a past history of coronary artery stenting. All of these should be regarded as contraindications to the use of apraclonidine or brimonidine.

The use of "argon"/green laser iridoplasty in early management of raised IOP for patients presenting with acute angle-closure crises was studied in an RCT which randomised patients to receive either laser iridoplasty or topical pilocarpine and timolol after all patients had received systemic acetazolamide. The trial found that the intraocular pressure fell more quickly in the group that underwent laser iridoplasty, but there was no difference between the two groups by two hours. [42] The interpretation of this trial differs around the world. There is no clear consensus that laser iridoplasty should be deployed as an immediate management in acute angle closure. However, it could be used as a second line treatment if the patient is unresponsive to topical medication and systemic acetazolamide after two hours, and possibly for patients with hazy corneas (e.g., due to oedema) that makes laser iridotomy technically not possible to conduct.

If a patient remains unresponsive to medication and laser iridoplasty, then diode laser cycloablation treatment is frequently very effective in controlling intraocular pressure. Emergency trabeculectomy is not advised. Limbal paracentesis has been reported as a management option which can rapidly achieve intraocular pressure lowering. However, anecdotally, this technique can lead to severe complications.

A randomized, controlled trial compared the efficacy of phacoemulsification and intraocular lens implant (phaco/IOL) with laser peripheral iridotomy (LPI) performed on people presenting with AAC within 1 week of presentation. People who had responded to medical treatment such that intraocular pressure (IOP) was ≤30 mmHg within 24 hours, and had cataract with visual acuity of ≤6/15 were enrolled. The 2-year cumulative survival was 61% and 89% for the LPI and phaco/IOL groups, respectively (P = 0.034), indicating that phaco/IOL may be superior to LPI in stabilizing IOP. [43]

Practice point
Consider the possibility of secondary (lenticular or retrolenticular) mechanisms of angle-closure. These cases typically present with asymmetrical central anterior chamber depth. These cases should be treated with mydriasis and not pilocarpine.

- 1st Line: Medical treatment with systemic acetazolamide, topical pilocarpine and other ocular hypotensive medication together should be given immediately in cases of acute primary angle closure. Topical steroids, oral analgesia and antiemetics (as required) should also be given.
- 2nd Line: Argon/green laser iridoplasty should be considered when medical treatment fails to break the attack **(Evidence/recommendation: Moderate; Weak)**
- Cyclodiode laser should be considered for cases refractory to both medical therapy and ALPI. **(Evidence/recommendation: Low; Strong)**
- Laser iridotomy or surgical iridectomy should be attempted in both eyes following resolution of the initial attack of acute angle closure **(Evidence/recommendation: Low; Strong)**
- Paracentesis has no proven role in the management of acute angle closure and may cause harm. **(Evidence/recommendation: Low; Strong)**
- In patients with cataract who experience acute angle closure, early phacoemulsification should be offered once intraocular pressure is controlled and the cornea is clear, approximately 1 to 4 weeks after presentation. **(Evidence/recommendation: Low; Strong)**

4.5 Surgery

- Clear lens phaco is superior to PI and is advised as primary intervention in PACG. **(Evidence/recommendation: High: Strong)**
- Phacoemulsification and goniosynechialysis (GSL) surgery does not reduce need for anti-glaucoma eyedrops versus phaco alone **(Evidence/recommendation: Moderate; Weak)**
- Phacoemulsification clear lens extraction/cataract surgery is preferred to trabeculectomy and phaco-trab in PACG on the basis of safety, but trabeculectomy or phacotrabeculectomy may be considered for severe disease **(Evidence/recommendation: Moderate; Weak)**
- Early phaco may be of more benefit than PI in patients with AAC and PACG with cataract **(Evidence/recommendation: Moderate; Weak)**

In patients with co-existing cataract and angle-closure disease, lens extraction is the initial treatment option for the management of early to moderate PACG. [44 45]

Two small RCTs have compared phacoemulsification alone versus phacotrabeculectomy with mitomycin-C for patients with PACG and cataract. A randomised controlled study on **medically controlled PACG with coexisting cataract**, found that phacoemulsification alone was effective in terms of decreasing IOP and reducing the requirements of postoperative glaucoma medications at 2 years. There were no significant differences in terms of IOP, visual acuity and progression of visual field between the two treatment groups. The phaco-trabeculectomy group required less topical medications in the 2-year period compared to the phacoemulsification alone group but experienced more complications. [46]

For **medically uncontrolled PACG with coexisting cataract**, phaco-trabeculectomy gave lower postoperative IOP and lower glaucoma medication usage than phacoemulsification alone in the 2-year follow-up period. However, phaco-trabeculectomy was again associated with more complications compared to phacoemulsification alone. [47]

Clear lens extraction (CLE) can be considered for the initial management of mild to moderate PACG, as well as PAC with IOP > 30 mmHg, for patients over 50 years of age. In the EAGLE trial, CLE resulted in slightly better IOP lowering, reduced medication use and subsequent glaucoma surgery, improved quality of life, and cost effectiveness compared to LPI. As the study was carried out in the UK and East Asia, the implications for non-Chinese/non-European populations are uncertain. Additionally, it should be noted that lens extraction can be more complicated intraoperatively and postoperatively than for routine eyes.

In medically uncontrolled PACG eyes without cataract, **trabeculectomy with mitomycin C** may be indicated, particularly in younger patients with accommodative ability. In a small RCT comparing the efficacy of phacoemulsification versus trabeculectomy with mitomycin-C in medically uncontrolled PACG eyes with clear lens, trabeculectomy group was found to be more effective than phacoemulsification, requiring on average 1.1 fewer drugs after surgery. Surgical complications were substantially higher in the trabeculectomy group than among those undergoing phacoemulsification (44% vs. 4% respectively). There were no differences between the two treatment groups in number of additional surgical interventions at 2 years, although one third of patients undergoing trabeculectomy developed significant cataract within this timeframe. [48]

However, in cases of advanced PACG, uncontrolled IOP and concurrent cataract, primary trabeculectomy with mitomycin-C may be a viable option. The sequence of cataract and glaucoma surgery need to be considered carefully. The benefits of sequential surgery versus combined phaco-trabeculectomy in more severe or advanced disease remain unclear.

Modifications to the surgical technique of trabeculectomy in PACG have been suggested to avoid complications and improve the outcome. This includes making a more anteriorly placed sclerostomy; avoiding extreme IOP fluctuations during the intraoperative period by maintaining a deep anterior chamber and preplacement of sutures before the sclerostomy; avoiding post-operative hypotony by applying multiple, tight scleral flap sutures, conservative suture lysis or removal, as well as the use of cycloplegic therapy.

Minimally invasive glaucoma surgery: MIGS devices are not licenced for use in angle-closure glaucoma in the UK. Even though minimally invasive glaucoma surgical devices (MIGS) have a generally favourable safety profile, their effectiveness is insufficiently proven in angle-closure disease. [49 50 51] Several types of MIGS are currently in the market with the majority aiming to bypass the trabecular meshwork through a small device, often implanted during cataract extraction. In PACG eyes, presence of PAS can make the intervention difficult or impossible to do.

Glaucoma drainage device surgery alone
Glaucoma drainage device (GDD) surgery can be considered in individuals with sufficiently deep anterior chambers. In pseudophakic eyes with a shallow chamber, tube placement can be performed in the ciliary sulcus. There is a lack of evidence comparing the results of GDD with trabeculectomy in PACG.

4.6 Laser

- Prompt laser PI is advised in AAC and fellow eyes **(Evidence/recommendation: Low; Strong)**
- Laser peripheral iridoplasty offers no clear benefit in addition to PI in PACG **(Evidence/recommendation: High; Strong)**
- SLT after PI offers no clear benefit for IOP control **(Evidence/recommendation: Moderate; Weak)**
- Location and size of PI do not seem to have any impact on the rate of dysphotopsia **(Evidence/recommendation: Moderate; Weak)**
- Sequential argon/YAG PI is preferred in dark irides (for example, those of Asian/African descent) **(Evidence/recommendation: Moderate; Strong)**

Laser peripheral iridoplasty
A Cochrane review did not find sufficient evidence to recommend the use of laser iridoplasty in non-acute cases of PAC and PACG. However laser peripheral iridoplasty can be an effective procedure to break iridotrabecular contact in an acute attacks of angle closure. [42] Iridoplasty can be used as a first-line treatment or in cases that are refractory to medical treatments. Iridoplasty does not replace iridotomy as the main intervention for the treatment of angle closure.

Laser trabeculoplasty

Laser trabeculoplasty for PAC and PACG where the angle opens after iridotomy has overall poor long-term success rates and is currently not recommended for any form of PAC or PACG. [52 53]

Laser Cyclophotocoagulation

There are few studies specifically evaluating trans-scleral cyclophotocoagulation (TSCPC) and micropulse TSCPC in angle-closure patient. [54] It is a treatment which is usually reserved for cases of refractory glaucoma. Micropulse TSCPC is a relatively new technique, using short bursts of energy that are delivered to the ciliary body, generating thermal energy for coagulation. Evidence of the effectiveness of micropulse TSCPC for PACG is lacking. Similarly, there is no evidence to support endoscopic cyclophotocoagulation for PACG. Case series suggest that TSCPC can help to control the IOP in acute angle closure attacks that do not respond to standard treatment. [55]

4.7 Medication

- Prostaglandin monotherapy is effective in lowering IOP in PACG, and out-performs timolol. **(Evidence/recommendation: High; Strong)**
- There is no benefit of one PGA over another **(Evidence/recommendation: Moderate; Weak)**

Medical treatment for PACG is similar to that of open angle glaucoma, including beta blockers, prostaglandin analogues, alpha-agonists and carbonic anhydrase inhibitors. Studies have shown a higher efficacy of prostaglandin analogues compared to timolol monotherapy for IOP lowering in eyes with PACG post-LPI. [56] While miotics such as pilocarpine may be beneficial in PACG with non-pupil-block/plateau iris, it is not extensively used in angle closure disease due to its adverse effects profile.

z. Management in different racial groups.

- While there is no evidence supporting differences in management, clinicians should be aware of racial differences including underlying biometric and iris anatomy variation. **(Evidence/recommendation: Moderate; Strong)**

Anyone who has operated on the anterior segment of the eye will be well aware of the differences of in behaviour of the iris between blue-eyed Caucasians and brown-eyed Asian and Africans. The stiffer, thicker iris in Asians and African people makes surgery and post-operative management more forgiving after trabeculectomy. However, no race-specific management pathways have been developed or proven in objective research.

Research need

- The frequency of angle-closure disease in people of African and Caribbean heritage is poorly understood.
- The need for different care pathways in different racial groups is unclear

4.8 Follow up

aa. How to manage residual iridotrabecular contact (ITC)

- No evidence supports further interventions for ITC alone. It may be used to risk-stratify follow-up for PAC disease after PI.
- Additional interventions are not recommended unless there is a documented increase in IOP, worsening GON or recurrent symptomatic attacks.

Non-synechial residual iridotrabecular contact (ITC) is encountered in between 20% and 33% of cases following laser peripheral iridotomy, and is rarely seen after phacoemulsification. There is no evidence to guide management of this finding. Management of these cases is dictated by the IOP, the presence of glaucoma, and the visual function of both the affected and fellow eyes.

4.9 Management of symptomatic cataract in angle-closure

- Phacoemulsification and IOL should be offered in line with cataract surgery guidance
- Excess risk for patients with an axial length of < 21.00 should be explained (see nanophthalmos – below) **(Evidence/recommendation: Moderate; Strong)**
- There is no evidence to recommend laser peripheral iridotomy prior to phacoemulsification and IOL. **(Evidence/recommendation: Low; Weak)**

Patients with visually significant cataract should be treated in line with current cataract surgery guidance. Studies of the genetics of primary angle-closure glaucoma suggest that collagen abnormalities are a key determinant of the disease. Syndromic connective tissue diseases are well known to be associated with angle-closure (e.g. Marfan, Ehler Danlos). These may make surgery more technically challenging. The higher prevalence of hypermetropia means that some patients may have undetected amblyopia. Nanophthalmic patients may have foveal hypoplasia. Consequently, the visual prognosis may be limited by these conditions. In patients with shorter axial length, the complication rate doubles with every 1 mm short axial length below 21mm. [57] This should be discussed and documented as an excess risk. Ocular biometry in very small eyes will be (far) less accurate, and this should be taken into account when choosing an IOL, and discussing likely refractive outcome.

Surgical outcomes in patients with axial length > 21mm and no significant ocular comorbidity is generally good, although cases with angle-closure are not recommended for early years trainee surgeons.

Laser iridotomy is not recommended as routine pre-surgical care, but patients with documented pressure instability or suspected symptomatic disease (intermittent angle-closure) should be dilated immediately before surgery, without an undue wait.

4.10 How to handle pupil dilation in suspected or established angle-closure

- The risk of acute angle closure after dilation is low in the general population. **(Evidence/recommendation: High; Strong)**
- Among diabetics, there may be a greater risk of AAC from repeat dilation for diabetic retinopathy screening examinations. **(Evidence/recommendation: Moderate; Strong)**
- See section on PACS regarding the role of laser PI in people requiring regular pupil dilation

Dilation of the pupil is an integral part of a comprehensive eye examination. The examination is frequently required in management of common systemic and ophthalmic conditions such as age-related macular degeneration, retinal vascular occlusions and diabetic retinopathy. As such, the outcome of a dilated retinal examination may have implications beyond the sight of the individual.

These considerations are balanced against the very low risk of an acute episode of angle-closure (AAC) resulting from dilation during a routine eye examination, which are somewhere between 1/5,000 and 1/10,000 across the general adult population. Consequently, the balance between risk and benefit seems heavily in favour of continuing with routine dilation in most patients. [58]

Diabetic retinopathy screening does seem to constitute a special case, accounting for more cases of AAC in the UK than any other identifiable health event. [19] The need for repeat examinations creates and additive risk and as such, there is probably a benefit for identifying diabetics at risk of angle-closure, and arranging a glaucoma specialist review to consider prophylactic laser iridotomy for these patients.

In patients with established or probable angle-closure, pupil dilation can be safely performed in most cases using tropicamide alone, and prescribing PO acetazolamide 250mg on leaving the department, and another dose at bedtime that night (unless there is a contra-indication to using this drug). Pilocarpine should not be used to re-constrict the pupil after dilation as this may splint the pupil in a mid-dilated position and increase the risk of angle-closure.

4.11 Aqueous misdirection/malignant glaucoma – diagnosis, prevention, management

The diagnosis should be considered in any patient with sudden shallowing of the anterior chamber, especially occurring post-operatively. The intraocular pressure may be normal in some cases. Choroidal expansion and resistance to flow of aqueous from the posterior to the anterior segment leads to forward displacement of the irido-lens diaphragm and closure of the anterior chamber angle. Short axial length, an angle-closure diagnosis and lens status (being phakic) are risk factors. Good evidence on prevention and management is lacking.

Initial medical treatment is with cycloplegics (atropine or cyclopentolate) and aqueous production suppressants given systemically and/or topically, followed by hyperosmotics, such as mannitol (if no contraindications). A patent peripheral iridotomy must be performed if not already present.

In phakic eyes, pars plana vitrectomy with or without lens extraction may be needed. In pseudophakic eyes Nd:YAG laser vitreolysis/capsulotomy may be tried. Zonulo-hyaloido-vitrectomy via anterior chamber, through a peripheral iridectomy or iridotomy via the anterior chamber, [59] is an effective option. Alternatively, a pars plana approach is also possible.

Diode laser cyclophotocoagulation is an effective alternative treatment in many cases. [60]

4.12 Management differences in small eyes (nanophthalmos)

We use the term nanophthalmos to indicate eyes with an axial length of less than 20.00 mm

- Patients with nanophthalmos should be counselled of the risks of lens / cataract surgery as complications may occur in 30% of cases or more. These include aqueous misdirection, zonular dialysis, cystoid macular oedema and choroidal effusions. **(Evidence/recommendation: Moderate; Strong)**
- Accurate biometry is challenging, and the risk of refractive surprise should be clearly explained. **(Evidence/recommendation: Moderate; Strong)**
- In eyes with nanophthalmos undergoing lens or cataract extraction consideration should be given for performing a surgical iridectomy at the time of surgery to reduce the risk of post-operative pupil block, and to assist with management of aqueous misdirection if this should occur. **(Evidence/recommendation: Low; Strong)**
- A significant proportion of patients with nanophthalmos who have lens or cataract surgery may not achieve BCVA > 6/12 due to underlying amblyopia or foveal hypoplasia **(Evidence/recommendation: Low; Weak)**
- Consideration should be given to performing pars plana vitrectomy at the same time as phacoemulsification in very small eyes with very shallow anterior chambers following discussion with a vitreo-retinal surgeon. **(Evidence/recommendation: Low; Weak)**

4.13 Differences in management of four levels of "block": pupil, ciliary processes/iris crowding, lens (incl. phacomorphic/white cataract) and retrolenticular.

The concept of different levels of obstruction to aqueous circulation, each of which may trigger a rise in IOP is useful in determining the most appropriate intervention, especially in atypical cases. Pupil block and peripheral iris crowding of the drainage angle account for the majority of angle-closure disease, and are considered a "primary" phenomenon. In contrast, lenticular and retro-lenticular causes of aqueous obstruction are viewed as "secondary" disease.

Lenticular or "lens-induced" should be clearly differentiated from "common" primary angle-closure in which the size and position of the lens results in a shallow anterior chamber and a crowded angle. In "secondary" lens-induced angle-closure, the lens is either "white or wobbly". Surgical lens extraction may be complicated, frequently requiring mechanical dilation of the pupil, capsular staining, capsular tension rings and possibly pars planar instrumentation to remove a dropped nucleus.

Retro-lenticular causes of angle-closure typically originate from massive vitreous or sub-retinal haemorrhage, inflammatory effusions or tumours.

Practice point
If secondary lenticular/retro-lenticular angle-closure presents with acute symptoms or high pressure, the initial management should be dilation of the pupil with atropine +/- phenylephrine.

PRIMARY = PILOCARPINE
SECONDARY = CYCLOPLEGIA

2. "Atypical disease" – drug induced

Antidepressant medication (SSRI and tricyclics) usage is associated with an increased risk of angle-closure disease. Patients should be advised of this excess risk, and to discuss the need for this medication with the prescribing physician. [61]

Idiosyncratic reactions to drugs such as topiramate may cause atypical mechanisms such ciliary rotation due to supraciliary effusions. [41] The possibility of changing to alternative medications should be discussed with the prescribing physician.

4.14 Non-penetrating glaucoma surgery and MIGS in angle-closure

- There is no useful evidence on the use of non-penetrating and MIGS surgery in angle-closure

Minimally invasive glaucoma surgery (MIGS) is increasingly promoted by the medical devices industry. Their use remains unproven in PACD and PACG. [49, 50, 51] These devices are not licensed for use in angle-closure in the UK.

The role of goniosynechialysis (GSL) as an adjunct to phacoemulsfication has been tested in 7 small studies which were subjected to meta-analysis, which suggested that GSL might contribute to better pressure control. [62] A larger randomised controlled trial did not identify any benefit from GSL. [29]

5 Risks, Benefits and Limitations

5.1 Benefits and risks

PACG has the potential to lead to severe, irreversible loss of vision. Consequently, the condition must be managed carefully. Changes to management must be approached with caution as there will inevitably be unintended consequences. Over the last decade, there has been growing awareness that the resource implications for actively managing people with narrow angles (primary angle-closure suspects) – believed to be at undefined future risk of PACG, may be excessively cautious; many people in the UK are referred to the hospital eye service for prophylactic treatment. This caution is exercised in the setting of individual risk being low, and the risk in the wider population is known to be falling. The large number of "at risk" individuals being referred represents an "opportunity cost", absorbing capacity that that could be allocated to other patients. The events of the first 6 months of 2020, with COVID19 causing an unprecedented slowdown in chronic disease healthcare activity, bring the risks, benefits and opportunity costs into sharper focus. Hospital capacity will be sorely tested as services accelerate in the recovery phase. It is now more vital than ever that finite resources should be directed towards those in greatest need. It is therefore timely to examine the evidence for most effective and efficient management of PACG.

The dilemma now faced in PACG mirror the numerically bigger problem in POAG care – how to we identify those at greatest risk, and deploy early, definitive treatment while avoiding treating those who will not progress to functionally significant visual loss within their lifetime? In focusing attention on those with the highest risk of sight loss, it important to make it very clear that the recommendations for clear lens extraction surgery in people who meet the enrolment criteria for the EAGLE trial does not declare "open season" for surgery on all patients with narrow angles. This caveat should be made particularly clear for patients and clinicians in the private sector. While some latitude and clinical judgement is appropriate, we would expect that all decisions to perform lens extraction for control of angle-closure disease should involve a consultant with a specialist interest in glaucoma.

5.2 Limitations of the evidence

Much of the scientific data that informs the diagnosis and management of PACG emanates from East Asia, especially Singapore, Hong Kong and The Peoples' Republic of China. PACG is more common by a factor of 3 in these nations, and consequently carrying out research is made easier by the larger caseload, and the relative importance of the condition. In contrast, in the UK, PACG is less common than POAG, and regarded as a lower priority. However, the numbers of people identified as "at risk" is substantial. In developing these guidelines, we have drawn on much data from other nations. Although many studies have enrolled East Asian research participants, there are useful and valid messages for management of the multi-ethnic but predominantly white population of the UK. Foremost among these must be the evidence around the risk of incident angle-closure disease that threatens sight among primary angle-closure suspects – those people identified as having "narrow drainage angles" during an examination in an optometry practice or a general hospital eye clinic.

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7. Search strategies

Q1a

MEDLINE

1. glaucoma, angle-closure/ 2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. Terminology as Topic/
13. Disease Management/
14. (International society of Geographical and Epidemiological Ophthalmology).tw.
15. ISGEO.tw.
16. classification.tw.
17. (angle adj2 clos$ adj2 scor$).tw.
18. treat$ algorithm$.tw.
19. or/12-18
20. 11 and 19
21. chi.lg.
22. exp china/
23. (China or Chinese or India or Indian$).tw.
24. or/21-23
25. 20 not 24
26. exp case report/
27. (case adj2 report$).tw.
28. 26 or 27
29. 25 not 28

Embase

1. closed angle glaucoma/ or glaucomatous optic neuropathy/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. disease classification/
13. (International society of Geographical and Epidemiological Ophthalmology).tw.

14. ISGEO.tw.
15. classification.tw.
16. (angle adj2 clos$ adj2 scor$).tw.
17. treat$ algorithm$.tw.
18. or/12-17
19. 11 and 18
20. chinese.lg.
21. exp china/
22. (China or Chinese or India or Indian$).tw.
23. or/20-22
24. 19 not 23
25. exp case report/
26. (case adj2 report$).tw.
27. 25 or 26
28. 24 not 27
29. limit 28 to conference abstract status
30. 28 not 29

Q1b and Q1c

MEDLINE

1. glaucoma, angle-closure/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. prevalence/
13. Incidence/
14. (incidence or prevalence or surveillance).tw.
15. epidemiology/
16. epidemiological monitoring/
17. (aetiolog$ or etiolog$ or cause$ or causal).tw.
18. or/12-17
19. ((visual or vision or sight) adj2 (impair$ or loss$)).tw.
20. ((visual or vision or sight) adj2 morbid$).tw.
21. CVI.tw.
22. or/19-21
23. 18 or 22
24. exp Great Britain/
25. United Kingdom.tw.
26. Great Britain.tw.
27. Northern Ireland.tw.
28. (England or Scotland or Wales).tw.

29. or/24-28
30. Europe/
31. united states/
32. Canada/
33. or/30-32
34. 29 or 33
35. 11 and 23 and 34

Embase

1. closed angle glaucoma/ or glaucomatous optic neuropathy/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. prevalence/
13. incidence/
14. (incidence or prevalence or surveillance).tw.
15. epidemiology/
16. (aetiolog$ or etiolog$ or cause$ or causal).tw.
17. or/12-16
18. visual impairment/ep [Epidemiology]
19. ((visual or vision or sight) adj2 (impair$ or loss$)).tw.
20. ((visual or vision or sight) adj2 morbid$).tw.
21. CVI.tw.
22. or/18-21
23. 17 or 22
24. exp United Kingdom/
25. United Kingdom.tw.
26. Great Britain.tw.
27. Northern Ireland.tw.
28. (England or Scotland or Wales).tw.
29. or/24-28
30. Europe/
31. United States/
32. Canada/
33. or/30-32
34. 29 or 33
35. 11 and 23 and 34

Q1d

MEDLINE

1. glaucoma, angle-closure/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. risk factors/
13. (risk$ adj3 (factor$ or score$ or increase$)).tw.
14. (age$ adj3 risk$).tw.
15. ((women or female$ or gender$ or sex) adj3 risk$).tw.
16. ((family or families or relative$) adj3 risk$).tw.
17. ((Asia$ or China or Chinese of India$ or ethnicit$) adj3 risk$).tw.
18. or/12-17
19. hyperopia/
20. (hyperop$ or hypermetrop$).tw.
21. (far adj1 sight$).tw.
22. (long adj1 sight$).tw.
23. farsight$.tw.
24. longsight$.tw.
25. or/19-24
26. risk$.tw.
27. 25 and 26
28. 18 or 27
29. 11 and 28
30. exp case reports/
31. (case adj2 report$).tw.
32. 30 or 31
33. 29 not 32
34. (mouse or mice or rabbit or primate$).tw.
35. 33 not 34

Embase

1. closed angle glaucoma/ or glaucomatous optic neuropathy/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AACG or AcACC or APAC or CACG).tw.

9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. risk factor/
13. (risk$ adj3 (factor$ or score$ or increase$)).tw.
14. (age$ adj3 risk$).tw.
15. ((women or female$ or gender$ or sex) adj3 risk$).tw.
16. ((family or families or relative$) adj3 risk$).tw.
17. ((Asia$ or China or Chinese of India$ or ethnicit$) adj3 risk$).tw.
18. or/12-17
19. hypermetropia/
20. (hyperop$ or hypermetrop$).tw.
21. (far adj1 sight$).tw.
22. (long adj1 sight$).tw.
23. farsight$.tw.
24. longsight$.tw.
25. or/19-24
26. risk$.tw.
27. 25 and 26
28. 18 or 27
29. 11 and 28
30. exp case report/
31. (case adj2 report$).tw.
32. 30 or 31
33. 29 not 32
34. (mouse or mice or rabbit or primate$).tw.
35. 33 not 34
36. limit 35 to conference abstract status
37. 35 not 36

Q1e

MEDLINE

1. glaucoma, angle-closure/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. peripheral anterior synechiae.tw.
6. (glaucoma$ adj2 optic adj2 neuropath$).tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. Disease Progression/
13. (natural adj2 histor$).tw.
14. (disease adj2 (stage$ or course$ or level$ or progress$)).tw.
15. (glaucoma$ adj2 (stage$ or course$ or level$ or progress$)).tw.
16. untreated.tw.

17. no$ treat$.tw.
18. or/12-17
19. 11 and 18

Embase

1. closed angle glaucoma/ or glaucomatous optic neuropathy/
2. (angle adj1 closure adj1 glaucoma$).tw.
3. (angle$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
4. (glaucoma$ adj3 (occlud$ or narrow$ or width or close$ or closure)).tw.
5. (glaucoma$ adj2 optic adj2 neuropath$).tw.
6. peripheral anterior synechiae.tw.
7. or/1-6
8. (PAC or PACS or PACG or PACD or ACG or AAC or AcACC or APAC).tw.
9. (angle$ or glaucoma$).tw.
10. 8 and 9
11. 7 or 10
12. disease course/
13. (natural adj2 histor$).tw.
14. (disease adj2 (stage$ or course$ or level$ or progress$)).tw.
15. (glaucoma$ adj2 (stage$ or course$ or level$ or progress$)).tw.
16. untreated.tw.
17. no$ treat$.tw.
18. or/12-17
19. 11 and 18

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