Treatment of primary angle closure: What do the trials tell us?

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Angle closure: Definitions

Standardised definitions of disease (ISGEO 2002)

ITC (PACS)  Iridotrabecular contact

PAC  Primary angle closure

PACG  Primary angle closure glaucoma

ISGEO Diagnostic classification of glaucoma for prevalence surveys
Foster et al. BJO 2002
Angle closure: Management

Stages
- Acute angle closure
- Primary angle closure
- Primary angle closure glaucoma
- Asymptomatic narrow angles (ITC)

Treatment options
- Laser iridotomy
- Surgical iridectomy
- Iridoplasty
- Lens extraction
- Trabeculectomy
- Drops

Acute angle closure - Management

Acute attack broken
  ↓
  Oral diamox qds
  Topical IOP lowering treatment
    - Topical steroid 2 hrly
    - Pilocarpine both eyes
      ↓
  Laser iridotomy BOTH EYES

Acute attack not broken
  Diamox/ Mannitol iv
  Iridoplasty

WGA consensus statement:
"Laser iridotomy should be performed as soon as feasible in the affected eye(s), and should also be performed as soon as possible in the contralateral eye."
RCT of iridoplasty vs medical treatment for APAC

Mean IOP (mmHg) vs Time course in relation to treatment (HOURS)

- Immediate ALPI
- Medical treatment

Lam DS et al Ophthalmology 2002

Refractory acute angle closure

Urgent (24-48 hours)

- Lens extraction (General Anaesthesia)
  - Cyclodiode laser

1-2 months

- Trabeculectomy + MMC or tube
- Lens extraction +/- Goniosynechialysis or Trabeculectomy + MMC

*Manna A et al. EYE 2012
Asymptomatic narrow angles
(Iridotrabecular contact)

Treatment options:

1. Observe
2. Laser iridotomy
3. Cataract extraction: only when symptomatic

Laser peripheral iridotomy
Evidence supporting iridotomy?

Good evidence that protects eyes against acute angle closure

- Fellow eye data: Caucasian eyes
  - 50% untreated → APAC
  - 2% iridectomy → APAC

Fellow eye data: Asian eyes
  - No APAC in 71 fellow eyes treated with PI at 4 years

Lowe RF, Snow JT
Ang L, 2000

Laser peripheral iridotomv for the prevention of angle closure: a single-centre, randomised controlled trial

- Guangzhou, China
- Randomised controlled trial
- Subjects 50-70 years old
- Asymptomatic narrow angle (ITC in 2 or more quadrants)
- Identified through community screening
- Randomised one eye to laser iridotomy and fellow eye control

Primary outcome:
- Incident primary angle closure disease: elevated IOP, PAS or AAC
- Follow up 6 years
Results

4.19 per 1000 eye-years (PI)
7.97 per 1000 eye-years (control)

Hazard ratio = 0.53 (95% CI: 0.3-0.92, p =0.024)
No sight –threatening events

Baseline Findings associated with endpoint

<table>
<thead>
<tr>
<th>Variable</th>
<th>Eyes that did</th>
<th>Eyes that did not</th>
<th>Hazard ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate model</td>
<td>reach endpoint</td>
<td>reach endpoint</td>
<td>34.5%</td>
<td>0.033</td>
</tr>
<tr>
<td>Randomly assigned to laser peripheral iridotomy</td>
<td>34.5%</td>
<td>34.5%</td>
<td>0.033</td>
<td>0.033</td>
</tr>
<tr>
<td>Multivariate models</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years (per year older)</td>
<td>69.9 (1.0)</td>
<td>59.9 (1.0)</td>
<td>1.02 (1.01-1.03)</td>
<td>0.005</td>
</tr>
<tr>
<td>Randomly assigned to laser peripheral iridotomy (or control)</td>
<td>54.5%</td>
<td>54.5%</td>
<td>0.032</td>
<td>0.032</td>
</tr>
<tr>
<td>Baseline intraocular pressure, mm Hg (per 1 mm Hg increase)</td>
<td>15.76 (1.40)</td>
<td>15.06 (2.43)</td>
<td>1.09 (0.99-1.19)</td>
<td>0.075</td>
</tr>
<tr>
<td>Total angle width, degree (per 1 degree increase)</td>
<td>4.82 (0.37)</td>
<td>5.36 (2.38)</td>
<td>0.93 (0.82-1.02)</td>
<td>0.008</td>
</tr>
<tr>
<td>Limbal anterior chamber depth, % (per 1% increase)</td>
<td>18.64 (8.41)</td>
<td>22.38 (2.56)</td>
<td>0.40 (0.34-0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cortical anterior chamber depth, mm (per 1 mm increase)</td>
<td>2.90 (0.24)</td>
<td>2.90 (0.24)</td>
<td>1.00 (0.99-1.02)</td>
<td>0.213</td>
</tr>
<tr>
<td>Lens thickness, mm (per 1 mm increase)</td>
<td>4.92 (0.97)</td>
<td>4.87 (0.92)</td>
<td>0.97 (0.93-1.01)</td>
<td>0.258</td>
</tr>
<tr>
<td>Endothelial phenotypic translocation, mm Hg (per 1 mm Hg increase)</td>
<td>27.7 (32.53)</td>
<td>41.7 (7.07)</td>
<td>1.04 (0.04-1.01)</td>
<td>0.486</td>
</tr>
</tbody>
</table>

All values are mean (SD) unless stated otherwise. Multivariable Cox proportional hazards models included laser peripheral iridotomy, age, gender, baseline intraocular pressure, and variables of interest. *Total angle width was calculated by the sum of Stiles, gradiants of all the quadrants (range from 0 to 180, loge number of Incus/sector angle). **Limbal anterior chamber depth wa measured by model 2.00 mm. ***Cortical anterior chamber depth and lens thickness were measured by ultrasonic A-Scan.****
**Singapore Asymptomatic narrow angles laser iridotomy study (ANA-LIS)**

476 subjects > 50 yrs
Bilateral ITC ≥ quadrants

<table>
<thead>
<tr>
<th>Iridotomy one eye</th>
<th>No intervention other eye</th>
</tr>
</thead>
</table>

5 yr follow up

- 25 (5.25%) progression
- 48 (10.08%) progression

Progression = PAS, ↑iop, acute attack, symptomatic angle closure, PACG
2 AAC in observation group, one in PI group

NNT to prevent progression = 20.7

*Baskaran M, Sasikumar R, Wong HT et al. ARVO 2016*

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**Impact on clinical practice**

- Incidence of angle closure disease in individuals with asymptomatic narrow angles is **very low**
- Benefit of prophylactic iridotomy is limited
- Laser iridotomy for all narrow angle patients is **NOT** indicated
- Assess risk factors and discuss with patient:
  - Diabetics/ frequent mydriatic exam
  - Angle width and mechanism
  - Family history of AAC
  - Other medications eg anti anxiety medication
  - Clinical judgement
Example: 53 yr old man

- Left amblyopia, 270 ° ITC both eyes
- Mother Acute angle closure
- Offer PI

Example: 64 yr old woman

- ITC one quadrant
- Early cataract
- Watch
PAC and PACG

Treatment options:

1. Laser iridotomy
2. Laser iridoplasty
3. Eye drops
4. Lens extraction

Argon laser peripheral iridoplasty
ALPI for PAC (G) : RCT

<table>
<thead>
<tr>
<th>Iridoplasty</th>
<th>PG analogue</th>
</tr>
</thead>
<tbody>
<tr>
<td>51 eyes</td>
<td>55 eyes</td>
</tr>
</tbody>
</table>

80 subjects (106 eyes)
ITC ≥ 180° post PI
IOP > 21mmHg

Repeat x1 if IOP still or ITC at 1-3 months

1 yr follow up

35% complete success
35% qualified success
30% failure

85% complete success
7.5% qualified success
7.5% failure

Change in IOP at 12 months: ALPI: -4.9mmHg (3.5-6.3)
Meds: -6.1mmHg (5.1-7.1) (p<0.001)


Lens extraction
Phaco vs Phaco trab trial
Tham CC et al, Ophthalmol 2009

Medically uncontrolled PACG

Phaco
27 eyes

Phaco + Trab
24 eyes

- IOP lower in Phaco + trab
- ↓ meds required for phaco + trab
- 4 (14.8%) in phaco arm → trab

Complication rate:
- phaco only = 8.1%
- phaco + trab = 26.2% (p = 0.007)

The Effectiveness of Early Lens Extraction for Primary Angle Closure Glaucoma

Design: pragmatic RCT

PAC with IOP>30 mmHg or PACG

Phaco

Laser iridotomy

If both eyes eligible both received the same intervention
Index eye: the one with more advanced disease

Follow-up = 3 years

Inclusion criteria

• PACG with IOP ≥ 21 mmHg or PAC with IOP ≥ 30 mmHg
• At least 180 degrees of angle closure
• Newly diagnosed (up to 6 months)
• Age ≥ 50 years
• Phakic in affected eye (no cataract)

Exclusion criteria

• Previous acute angle closure
• Severe glaucoma (C/D ratio ≥ 0.9 or MD ≥ 15 dB)
• Symptomatic cataract
• Axial length ≤ 19 mm (nanophthalmos)
• Previous surgery (IOL, laser iridotomy)
• Increased surgical risk

Primary outcome

• Patient-centred: Health status (EQ-5D)
• Clinical: IOP
• Cost-effectiveness
Completed recruitment (n=419)

Asia – 7 sites

UK – 23 sites

Australia – 1 site

Baseline characteristics (n=419)

- Race: Chinese = 121 (29%)
- Age: 67.0 (+/- 9.8) years
- EQ-5D: 0.871 (+/- 0.18)
- Diagnosis: PAC= 157 (37%), PACG = 261 (62%)
- IOP: 28.9 (+/- 9.7) mmHg
- Humphrey MD: -4.2 (+/-6.0) dB
805 patients assessed for eligibility

419 enrolled

419 randomised

208 assigned to lens extraction

211 assigned to laser peripheral iridotomy

1 participant did not get the intervention (cross-over)

204 included in the intention-to-treat analysis

205 included in the intention-to-treat analysis

EAGLE study profile

Primary outcome: EQ-5D

<table>
<thead>
<tr>
<th></th>
<th>Lens extraction</th>
<th>Laser PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D score</td>
<td>N</td>
<td>mean (SD)</td>
</tr>
<tr>
<td>Baseline</td>
<td>204</td>
<td>0·87 (0·19)</td>
</tr>
<tr>
<td>36 months</td>
<td>176</td>
<td>0·87 (0·21)</td>
</tr>
</tbody>
</table>
### Primary clinical outcome: IOP

<table>
<thead>
<tr>
<th>IOP (mmHg)</th>
<th>Lens extraction</th>
<th>Laser PI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>mean (SD)</td>
</tr>
<tr>
<td>Baseline IOP</td>
<td>208</td>
<td>29·5(8·2)</td>
</tr>
<tr>
<td>36 months IOP*</td>
<td>182</td>
<td>16·6 (3·5)</td>
</tr>
</tbody>
</table>

*p = 0·004

*Includes patients who had glaucoma surgery during the 3-year follow-up

### Medications at 36 months

<table>
<thead>
<tr>
<th>Number of medications</th>
<th>Lens Extraction</th>
<th>Laser PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 medications, N (%)</td>
<td>126 (60·6%)</td>
<td>45 (21·3%)</td>
</tr>
<tr>
<td>1 medications, N (%)</td>
<td>33 (15·9%)</td>
<td>67 (31·8%)</td>
</tr>
<tr>
<td>2 medications, N (%)</td>
<td>15 (7·2%)</td>
<td>46 (21·8%)</td>
</tr>
<tr>
<td>3 medications, N (%)</td>
<td>3 (1·4%)</td>
<td>19 (9·0%)</td>
</tr>
<tr>
<td>4 medications, N (%)</td>
<td>1 (0·5%)</td>
<td>4 (1·9%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0·4 ± 0·8</td>
<td>1·3 ± 1·0</td>
</tr>
</tbody>
</table>
### Intra-operative* complications

<table>
<thead>
<tr>
<th></th>
<th>Lens extraction (N=208)</th>
<th>Laser PI (N=211)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior capsule rupture</td>
<td>2 (1·0%)</td>
<td></td>
</tr>
<tr>
<td>Iris prolapse</td>
<td>2 (1·0%)</td>
<td></td>
</tr>
<tr>
<td>Vitreous loss</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
<tr>
<td>Broken haptic</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
<tr>
<td>Bleeding or haemorrhage</td>
<td>16 (7·6%)</td>
<td></td>
</tr>
<tr>
<td>*Pre-operative attack angle closure</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
</tbody>
</table>

### Post-operative complications

<table>
<thead>
<tr>
<th></th>
<th>Lens extraction (N=208)</th>
<th>Laser PI (N=211)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flat anterior chamber</td>
<td>2 (1·0%)</td>
<td>1 (0·5%)</td>
</tr>
<tr>
<td>Retinal detachment or tear</td>
<td></td>
<td>1 (0·5%)</td>
</tr>
<tr>
<td>Malignant glaucoma</td>
<td>1 (0·5%)</td>
<td>2 (1·0%)</td>
</tr>
<tr>
<td>Corneal decompensation</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
<tr>
<td>Macular Oedema</td>
<td>5 (2·4%)</td>
<td>3 (1·4%)</td>
</tr>
<tr>
<td>IOP spike</td>
<td>2 (1·0%)</td>
<td>5 (2·4%)</td>
</tr>
<tr>
<td>Post-operative inflammation</td>
<td>5 (2·4%)</td>
<td>1 (0·5%)</td>
</tr>
<tr>
<td>Central retinal vein occlusion</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
<tr>
<td>Dysphotopsia</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
<tr>
<td>Posterior vitreous detachment</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
<tr>
<td>Macular hole</td>
<td>1 (0·5%)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

- Initial lens extraction for PACG and PAC with high IOP (>30mmHg) is associated with better clinical and patient-reported outcomes than laser PI.
- Initial lens extraction for PACG and PAC with high IOP is likely to be cost-effective.
- Lens extraction has a risk of PC rupture and other complications: individualised decision making!
- (EAGLE does not support that we must do lens extraction in all, it is an option)
- EAGLE results not applicable to ITC (Asymptomatic narrow angles only)
- Note IOP cut off of >30mmHg for PAC patients – if IOP <30 discuss with patient.

The effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma: a randomized controlled trial (EAGLE). The Lancet, 2016.

Summary - Indications for iridotomy

- Acute angle closure – affected and fellow eye.
- ITC – particularly high risk patients:
  - Diabetic
  - Family History
  - Travel frequently
- PAC with IOP <30mmHg (not fulfilling EAGLE criteria)
- PAC > 30mmHg and patient does not want surgery.
Indications for lens/ cataract surgery

- Symptomatic cataract
- PACG with IOP > 21mmHg RE
- PAC with IOP >30mmHg
- Refractory or recurrent acute or subacute angle closure

Is there a role for trabeculectomy in PACG?
32 yr old woman, blurred vision, PACG

Anterior segment OCT images

Right

Left
Summary - Advanced PACG, non-pupil block

- Age → Young (34)
- Lens status → Clear
- PAS - extent, onset → extensive, onset unknown
- Glaucomatous optic neuropathy → Advanced
- Chronicity of disease → Chronic
- Refractive error → None
- Biometry → AL 23.4 mm
- Mechanism of angle closure → Plateau/iris cysts
- Patient - circumstances and wishes → foreign service

Tips for trabeculectomy in angle closure

- Counsel patient re complications/ aqueous misdirection
- GA anaesthesia if small eye /high IOP
- Anterior chamber maintainer
- 3 - 4 tight releasable sutures
- No flow on table
- AC deep and formed at end of surgery
- Atropine at end of surgery
**Challenging case - 74 yr old man**

- 2nd opinion
- West African
- Advanced PACG
- Left phaco ➔ CMO
- Patient delayed intervention RE

- Maximum drops + Diamox
- + 5.0 D hypermetrope

**6/60 ph 6/24 RE**
- HM LE
- 360° PAS
- IOP 24mmHg RE, 54 mmHg LE
- Cataract

**WHICH OP ??**

10-2 VF Right eye
Thankyou