Key recent studies for glaucoma

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Πάντα ρέι καὶ οὐδὲν μένει

- Heraclitus of Ephesus.
  - 535-475 BC.
  - “Everything flows, nothing stands still”
  - Internal contradictions.
    - Dialectical thinking.
  - Died of dropsy at age 60.
- Late1980’s:
  - Harvard School of Public Health:
    - “No evidence for efficacy of Rx in Glaucoma”
POAG Basics.

  - Design and baseline description of the participants.

- **OHTS.** Arch Ophthalmol. 2000 Sep;118(9):1187-94.
  - Confirmation of VF defects is essential for distinguishing VF loss from long term fluctuation.

  - OHTS subjects have “thicker” corneas.
    - Whites thicker than blacks.
    - CCT affect tonometry, diagnosis & follow up.
POAG 

Basics.

• OHTS. Decrease IOP 20 % or observe?
  • AJO 120 No.6 June 2002.

  – Risk of developing glaucoma halved in susceptible individuals when IOP:
    • \( \leq 24 \text{ mm Hg} \) or 20% reduction from baseline average (min. 6 years follow up)
    • CCT powerful predictor.
    • Older age, higher IOP, greater PSD.
    • Larger c/d (V & H)
POAG

Basics.

• OHTS, cont.
  – “Susceptible individuals predictors”.
    • older age.
    • larger vertical or horizontal cup-disc ratio.
    • higher intraocular pressure.
    • greater pattern standard deviation.
    • thinner central corneal measurement.
    • At 7 yr, treated: 5% POAG, nonRx: 13%.
POAG
Basics.

  – Design, characteristics & purpose.
    • 607 pts OAG, initial Rx.
      – Medical Rx vs trabeculectomy.
      – 38 % blacks.

  – Quality of life issues.
POAG \textit{Basics.}

  - 609 newly diagnosed patients.
    - 4-5 years FU. Randomized to medical Rx or Trab (with or without 5FU).
    - IOPs
      - Medical Rx: 17-18 mm Hg (drop of 35\% from baseline).
      - Surgery: 14-15 mm Hg (drop of 48\% from baseline).
    - Similar VFs preservation.
POAG Basics.

- CIGTS, cont.
  - VA worse in surgery group (Cataract), but converging.
  - Worse prognosis older pts and in those with worse fields.
  - Meds vs Sx: Results similar in 5 yrs.

  - Quality of life.
    - Impact on surgical pts.
      - Ptosis.
      - FB sensation.

POAG

Basics

• Early Manifest Glaucoma Trial.
  - First to offer a control group with glaucoma.
    • Rx (medical) vs observation in early glaucoma.
      - 360º ALT + Betaxolol for 25 % IOP drop, 129 pts.
      - Observation 126 pts, Sweden & US.
  - At 8 years of follow up:
    • Overall progression 67%, Rx halved progression risk.
    • Progression factors: IOP, PXS, OU, Age, lower ocular systolic perfusion pressure, cardiovascular diseases, thinner corneas & disk hemorrhages.
POAG Basics

• Early Manifest Glaucoma Trial.
  – Median time for progression.
    • 48 months in control.
    • 66 months in treated.
  – This persistent separation between groups is damped by intervention over control group when progression is found.
  – 1 mm Hg drop = 12-13 % lowering risk.
POAG

Basics.

- Advanced Glaucoma Intervention Study,
  - Advanced POAG, 7 + years FUP.
  - 7 year outcome of laser or surgical treatment in patients with moderate to severe damage.
    - Possible sequences after MMT.
      - ALT, followed by Trab then Trab. ATT
      - Trabeculectomy followed by ALT, then Trab. TAT.

  - 789 eyes, 591 patients.

- Closure 3/31/2001
POAG

Basics

• Up to date 14 papers directly related to AGIS.
  • [http://www.cocnet.org/agis.html](http://www.cocnet.org/agis.html).
    – Medline links.
  • [http://spitfire.emmes.com/study/agi/resources/agis-bib.pdf](http://spitfire.emmes.com/study/agi/resources/agis-bib.pdf)
    – Complete bibliography.

• AGIS.
    • Description of study.
    • Visual Field scoring, 24-2
POAG

Basics

• AGIS cont.
    • Demographics, VF in blacks are worse.
    • Best sequence in blacks: ATT, whites: TAT.
    • Bleb encapsulation higher in males and after ALT.
    • VA improves after cataract sx.
    • Improvement greater when pre-op VA was lower.
POAG

Basics

  – Disease progression close to zero only if:
    • IOP below 18 mm Hg at all visits first six years of FUP.
    • Mean IOP during this period 12.3 mm Hg.
  – Lower VA:
    • Males.
    • Elderly.
    • Low Income.
  – Blacks vs White similar failure of Rx.
POAG Basics.

• AGIS, Cont.
  – Initial trab.
    • Better IOP control for whites.
    • VFs progression worse in blacks.
    • More cataracts in both.
    • May need medical therapy.
  – Whites on MMT.
    • Trab first.
  – Blacks on MMT.
    • ALT first.
POAG Basics

• AGIS cont.
    • After adjustment for age and DM, filtration sx increase risk of cataract by 78%.
    • Filtration sx is more effective in retarding glaucoma progression in whites than in blacks.
    • For optic nerve evaluations
      – High inter-observer agreement
      – Low inter-observer agreement.
    • ALT failure: younger age, high pre-laser IOP.
    • Filtration sx failure: younger age, high pre-op IOP, DM, post-op inflammation.
• AGIS cont.
    • Risk factors for sustained decreased VF.
      – Male
      – Better baseline VF.
      – Worse baseline VA in ATT.
      – DM in TAT.
    • Risk factors for sustained decreased VA.
      – Better baseline VA.
      – Older age.
      – Less formal education.
    • Long term visual functions better:
      – Blacks: ATT.
      – Whites: TAT.
### POAG Basics

- **AGIS cont.**
    - **Distinguishing progression in VF.**
      - Single confirmatory VF 6 months after worsening indicates a 72% probability if worsening is defined by at least 2 db of MD.
      - Two confirmatory tests increases probability to 84%.
    - 14a ? Ophthalmology. 2004 Sep;111(9):1627-35
      - **Factors that increase the odds of VF progression of at least 2 point locations within the same GHT.**
        - Older age at intervention: 1.30.
        - Increased number of interventions: 1.74.
        - Larger IOP fluctuations (SD of IOP): 1.31.
          - $< 3 \text{ mm Hg VF stable.}$
          - $\geq 3 \text{ mm Hg progression.}$
POAG Basics.

  - One eye treated, fellow eye control.
    - 7 + years FU.
    - 30 % drop from baseline for treated.
    - Deterioration ratio. Control vs. Treated, 3:1.
      - 35 % progressive vision loss in control.
      - 12% in treated group.
POAG Laser.

- Glaucoma Laser Trial (GLT).
  - ALT vs medical therapy as initial therapy.
    - Meds: Timolol, Pilocarpine, Propine.
    - Target 20% reduction IOP.
  - At 7 years, those who had laser first had slightly lower IOP (1.2 mm Hg), better VF and O.N.
    - 8% required surgery.
POAG

Laser.

- Glaucoma Laser Trial Follow up Study (GLTFS).
  - Extension of FUP for GLT.
  - ALT treated eyes had lower IOP
    - Better VF, better O.N.
  - Benefits small.
  - Just improve confidence in ALT.
POAG Surgery.

• 5- Fluorouracil Filtering Surgery Study.
  – 5 FU S/C for high risk filters.
    • 2 daily/wk then qd for second week (21 injections)
  – Improved significantly success rate of high risk cases.
  – Complications.
    • Wound leaks.
    • Corneal abrasions, erosions.
    • Hypotony, choroidal effusions & hemorrhages.
  – Basis for present adjuvant therapy (MMC etc).
Near future.

- Smaller studies.
- Role of the diurnal curve in the disease.
  - Variation is what is killing us.
- A glimpse:
  - OPH May 2006.
    - 30 medical & 30 surgical Rx OAG.
    - Average IOP
      - Medical $13.5 \pm 2.2$ mm Hg
      - Surgical $12.2 \pm 2.2$ mm Hg.
    - Surgical IOP had stat sign lower IOP at all points except 10 AM.