My Favorite Cases: A Clinical Guide to the Management of Glaucoma

My Favorite Cases

- Diagnosing and managing Ocular Hypertension and Glaucoma requires a series of decisions be made over the course of the lifetime of care
  - Is disease present?
    - What tests should be performed to aid in establishing diagnosis?
  - If disease is present, what type?
    - OHTN vs. Glaucoma
  - Is therapy required?
    - What therapy?
  - If glaucoma, what type?
    - Primary vs. secondary
    - Open vs. chronic angle closure
  - Grade severity of condition
  - Establish the target IOP
  - When should patient return?

What is Risk Assessment?

- 1961- Framingham Heart Study gave medicine the term “risk factor”
- Identification of risk factors for coronary artery disease
- Kamel et al. Factors of risk in the identification of coronary heart disease. The Framingham Study. Ann Int Medicine 1961; 55: 33-50.

How Can This Strategy Be Applied to Glaucoma?

- Identify patients at moderate to high risk of converting from ocular hypertension to glaucoma
- Direct therapy at those who are at greatest risk
- Which risk factors should be considered?

PERSPECTIVE

Risk Assessment in the Management of Patients With Ocular Hypertension

ROBERT N. WEINREB, MD, DAVID S. FRIEDMAN, MD, MPH, ROBERT D. FECHTNER, MD, GEORGE A. CIOFFI, MD, ANNE L. COLEMAN, MD, PHD, CHRISTOPHER A. GIRKIN, MD, MSPH, JEFFREY M. LIEBMANN, MD, KULDEV SINGH, MD, MPH, M. ROY WILSON, MD, MS, RICHARD WILSON, MD, AND WILLIAM B. KANNEL, MD, MPH

• PURPOSE: To develop a model for estimating the global risk of disease progression in patients with ocular hypertension and to calculate the "number-needed-to-treat" (NNT) to prevent progression to blindness as an aid to practitioners in clinical decision making.

• DESIGN: Development of a mathematical model for estimating risk of glaucoma progression.

• METHODS: Population-based studies of patients with ocular hypertension and glaucoma were reviewed by a panel of glaucoma specialists. Measures of disease progression risks derived from three long-term studies and assumptions based on the available data were used to estimate the risk of progression from ocular hypertension to glaucoma and glaucoma to unilateral blindness for untreated and treated patients over a 15-year period. Using these estimates, the NNT (1/absolute risk reduction on treatment) to prevent unilateral blindness in one patient with ocular hypertension was calculated.

• RESULTS: In untreated patients, the estimated risk of progression from ocular hypertension to unilateral blindness was 1.5% to 10.5% and in treated patients, the estimated risk of progression was 0.3% to 2.4% over 15 years. From these estimates, between 12 and 83 patients with ocular hypertension will require treatment to prevent one patient from progressing to unilateral blindness over a 15-year period.

• CONCLUSION: Global risk assessment that incorporates all available data plays a vital role in managing patients with ocular hypertension. A more precise understanding of long-term vision loss should be factored into decisions pertaining to the initiation of glaucoma therapy. Undoubtedly, these estimates will evolve and change with the availability of new population-based epidemiologic information and improvements in multivariable model testing. (Am J Ophthalmol 2004;138: 458–467. © 2004 by Elsevier Inc. All rights reserved.)

Biosketch and/or additional material at www.ajo.com
Accepted for publication April 27, 2004.

From the Hamilton Glaucoma Center, University of California, San Diego, La Jolla, California (R.N.W); Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland (D.S.F.); Institute of Ophthalmology and Visual Science, New Jersey Medical School—University of Medicine and Dentistry of New Jersey, Newark, New Jersey (R.D.F.); Devers Eye Institute, Discoveries in Sight, Legacy Health System, Portland, Oregon (G.A.C.); Jules Stein Eye Institute, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California (A.L.C.); Callahan Eye Foundation Hospital, University of Alabama at Birmingham, Birmingham, Alabama (C.A.G.); Manhattan Eye, Ear and Throat Hospital, and New York University School of Medicine, New York, New York (J.M.L.); Department of Ophthalmology, Stanford University Medical Center, Stanford, California (K.S.); Texas Tech University Health Sciences Center, Lubbock, Texas (M.R.W.); Jefferson Medical College and Wills Eye Hospital, Philadelphia, Pennsylvania (R.W.); Boston University School of Medicine, Boston, Massachusetts (W.B.K.).

Sponsored by Medical Intervention Systems, Parsippany, New Jersey, and supported by an unrestricted educational grant from Pharmacia Corporation, a Pfizer company.

Inquiries to Robert N. Weinreb, MD, Hamilton Glaucoma Center, University of California, San Diego, La Jolla, CA 92093-0946; fax: (858) 534-1625; e-mail: weinreb@eyecenter.ucsd.edu

THE PUBLICATION OF THE 5-YEAR RESULTS OF THE Ocular Hypertension Treatment Study (OHTS),[1] has caused some ophthalmologists to reassess the ways in which they evaluate and manage patients with ocular hypertension. According to the OHTS findings, the cumulative probability of developing glaucoma after 5 years is 9.5% in eyes with untreated ocular hypertension.[1,2] However, only a subset of patients who develop glaucoma is expected to lose functional vision during their lifetime. Despite the valuable contributions from the OHTS, particularly in identifying risk factors for progression to glaucoma, precise calculations of risk for disease progression to visual impairment in individual patients over given time periods, or perhaps more importantly over a patient's lifetime, are not yet available. Consequently, questions remain as to how best apply these new findings in deciding which patients to treat and how vigorously and when to initiate treatment.[3] A method of assessing risk of progres-

0002-9394/04/$30.00
doi:10.1016/j.ajo.2004.04.054

• PURPOSE: To develop a model for estimating the global risk of disease progression in patients with ocular hypertension and to calculate the "number-needed-to-treat" (NNT) to prevent progression to blindness as an aid to practitioners in clinical decision making.
• DESIGN: Development of a mathematical model for estimating risk of glaucoma progression.
• METHODS: Population-based studies of patients with ocular hypertension and glaucoma were reviewed by a panel of glaucoma specialists. Measures of disease progression risks derived from three long-term studies and assumptions based on the available data were used to estimate the risk of progression from ocular hypertension to glaucoma and glaucoma to unilateral blindness for untreated and treated patients over a 15-year period. Using these estimates, the NNT (1/absolute risk reduction on treatment) to prevent unilateral blindness in one patient with ocular hypertension was calculated.
• RESULTS: In untreated patients, the estimated risk of progression from ocular hypertension to unilateral blindness was 1.5% to 10.5% and in treated patients, the estimated risk of progression was 0.3% to 2.4% over 15 years. From these estimates, between 12 and 83 patients with ocular hypertension will require treatment to prevent one patient from progressing to unilateral blindness over a 15-year period.
• CONCLUSION: Global risk assessment that incorporates all available data plays a vital role in managing patients with ocular hypertension. A more precise understanding of long-term vision loss should be factored into decisions pertaining to the initiation of glaucoma therapy. Undoubtedly, these estimates will evolve and change with the availability of new population-based epidemiologic information and improvements in multivariable model testing. (Am J Ophthalmol 2004;138: 458–467.

Risk Assessment

- Consider number of risks individual has that puts them at risk for
  - conversion of ocular hypertension to the development of glaucomatous damage OR
  - from early glaucomatous damage to blindness
- Based upon evidence
- Studies include Ocular Hypertension Treatment Study
- What risk is too much and therapy is indicated prophylactically?
- Uses concept from Framingham Heart Study and Cardiovascular disease

Risk Assessment

- In cardiovascular disease, risk factors are evaluated to understand who is at risk for conversion to outcome such as MI or CVA
  - Risks include hypertension, obesity, elevated cholesterol, smoking, family history, sedentary lifestyle
- Similar risk factor assessment used to understand who may convert from OHTN to glaucoma

Risk Assessment

- Age
- IOP
- Corneal Thickness
- Vertical Cup/Disc Ratio
  - Optic Nerve healthy
- PSD Visual Field
  - Global Indice
  - Field full

Risk Assessment

- At what risk is therapy indicated to prevent undesirable outcome from occurring
- For glaucoma approximately 15% is consensus
- If cardiovascular disease, risk is approx 5%

Risk Assessment

- Risk Level Low < 5%
  - Monitor
- Risk Level Moderate 5-15%
  - Consider Therapy Discuss with patient
- Risk Level High >15%
  - Treat

The OHTS-EGPS Risk Calculator

Available for free as PDF download at

http://ohts.wustl.edu/risk/

Washington University in St. Louis
School of Medicine

GLAUCOMA 5-YEAR RISK ESTIMATOR

Università degli Studi di Milano Bicocca

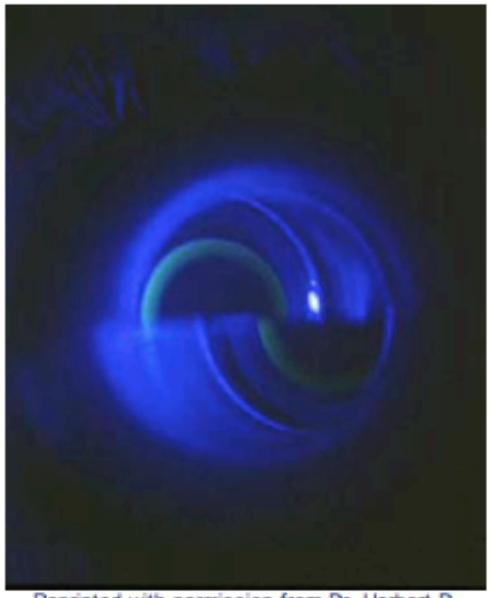
Istituto di Ricerche Farmacologiche Mario Negri

OHTS
Ocular Hypertension Treatment Study

Based on Results from
The Ocular Hypertension Treatment Study (OHTS)
and The European Glaucoma Prevention Study (EGPS)

New OHTS Calculator iPhone Application

European Glaucoma Prevention Study



Reprinted with permission from Dr. Herbert D. Riley, Indiana University, School of Optometry

We present a method for estimating the 5-year risk that an individual with ocular hypertension will develop primary open angle glaucoma (POAG).

The method may be useful to clinicians and patients in deciding the frequency of tests and examinations and the potential benefit of starting treatment.

More information is available in the manuscript, "A Validated Prediction Model for the Development of Primary Open Angle Glaucoma in Individuals with Ocular Hypertension," published in **Ophthalmology 2007; 114(1):10-19.** A list of publications from the OHTS and the EGPS is available in our **publications section.**

View the abstract here.

New OHTS Calculator iPhone Application

This website and glaucoma prediction model are not designed to, and do not, constitute medical advice. Results are not intended to be a substitute for professional medical evaluation, diagnosis, treatment or clinical judgement. The results of this prediction model are not deemed accurate for individual diagnosis. Any medical concerns regarding your eyesight should be directed to a medical professional.

Close Window

CONTINUOUS METHOD FOR ESTIMATING 5-YEAR RISK OF DEVELOPING POAG

INSTRUCTIONS:

1. Enter Patient Age and Ocular Data. (At least one measurement must be entered in each row.)
2. Click "Estimate Risk" to obtain the predicted 5-year risk of developing POAG.
3. Tooltips can be viewed by moving your mouse over any question mark.

FACTORS	RIGHT EYE MEASUREMENTS			LEFT EYE MEASUREMENTS		
? Age	1st	2nd	3rd	1st	2nd	3rd
? Untreated Intraocular Pressure *(mm Hg)*						
? Central Corneal Thickness *(microns)*						
? Vertical Cup to Disc Ratio by Contour						
? Pattern Standard Deviation ○ Humphrey *(dB)* ○ Octopus loss variance *(dB)*						

Estimate Risk | Print | Reset

Close Window

CONTINUOUS METHOD FOR ESTIMATING 5-YEAR RISK OF DEVELOPING POAG

INSTRUCTIONS:

1. Enter Patient Age and Ocular Data. (At least one measurement must be entered in each row.)
2. Click "Estimate Risk" to obtain the predicted 5-year risk of developing POAG.
3. Tooltips can be viewed by moving your mouse over any question mark.

FACTORS						
? Age 68	RIGHT EYE MEASUREMENTS			LEFT EYE MEASUREMENTS		
	1st	2nd	3rd	1st	2nd	3rd
? Untreated Intraocular Pressure *(mm Hg)*	25	25	27	24	25	26
? Central Corneal Thickness *(microns)*	515	520	522	515	518	515
? Vertical Cup to Disc Ratio by Contour	6.00			.7		
? Pattern Standard Deviation ⊙ Humphrey *(dB)* ○ Octopus loss variance *(dB)*	1.8	1.7		1.6	1.7	

Estimate Risk | Print | Reset

Life Expectancy Among Glaucoma Suspects

- American Geriatrics Society recommends that a patient's life expectancy be incorporated in medical decision making
- Calculating the benefits of treatment of a chronic disease needs to account for possibility that a patient will die before developing any symptoms from chronic disease

Life Expectancy Data

(*USA, 2002, all persons, median)*

Current Age	Years	Life Expectancy
45 yrs	34.8	79.9 yrs
65 yrs	18.3	83.3 yrs
85 yrs	6.1	91.1 yrs

DHHS. National Center For Health Statistics
http://www.cdc.gov/nchs/data/nvsr/nvsr53/nvsr53_06.pdf

Six Important Questions in Managing OHTN or POAG

- What is the risk to our patient's visual function if condition is not treated?
- If we accept that OHTN and glaucoma has a natural history, how early must we treat to alter natural history and preserve vision?
- What are the downsides to treatment?
- Which treatment is best?
- How are the results of the treatment best measured?
- What risk factors help most in making the best management decisions?

Five Rules for Assessment of the Optic Disc in Glaucoma

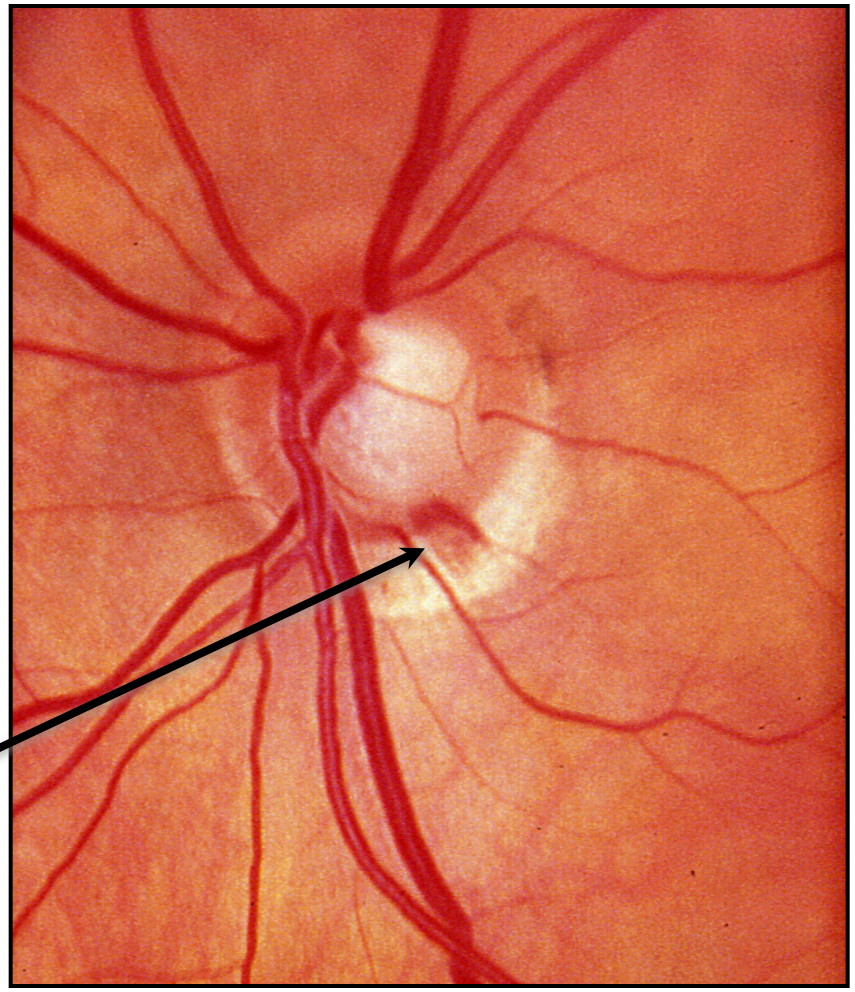
1 Observe the scleral Ring to identify the limits of the optic disc and its size

2 Identify the size of the Rim

3 Examine the Retinal nerve fiber layer

4 Examine the Region of parapapillary atrophy

5 Look for Retinal and optic disc hemorrhages



Initial Medical Management of OAG

- Before starting therapy
  - obtain several IOP readings
    - either done on one day (diurnal curve) or over 2-3 days at different times
    - need detailed pretreatment information
      - medical and ocular
  - grade severity of glaucoma
    - based upon nerve appearance, fields and highest IOP

Describe and Understand Condition

- Open vs. Narrow Angle
  - Chronic angle closure glaucoma resembles open angle forms
    - detect with gonioscopy
    - Asians
- Primary vs. Secondary forms
  - detect with slit lamp evaluation
  - secondary glaucomas

Clinical Correlations in Glaucoma

- Compare the visual field and optic nerve appearance
- Does the disc and visual field correlate?
  - Often the structure – function analysis does not correlate
- Does the comparison between the right and left eyes fit?
- Ask “How will optic nerve and visual field appear in twenty years”
- Lower target IOPs

Clinical Decisions in Glaucoma

- Target pressure
- Select therapy vs. No therapy
  - Medications
    - **Prostaglandins- most common first line agent**
    - Beta blockers
    - CAI
    - Adrenergic
  - Laser Trabeculoplasty
  - Filter Surgery

Topical Glaucoma Treatments

BRAND NAME/ MNFR	GENERIC NAME	CONCENTRATION/ BOTTLE SIZE
Beta Blockers Betagan/Allergan	levobunolol HCL	0.25% - 5mL, 10mL; 0.5% - 2mL, 5mL, 10mL, 15mL
Betimol/Vistakon	timolol hemihydrate	0.25% - 5mL; 0.5% - 5mL, 10mL, 15mL
Betoptic-S/Alcon	betaxaolol HCL	0.25% - 2.5mL, 5mL, 10mL, 15mL
Istalol/Ista	timolol maleate	0.5% - 5mL
Timoptic/Aton Pharma	timolol maleate	0.25% - 5mL, 10mL, 15mL; 0.5% - 5mL, 10mL, 15mL
Timoptic (preservative-free)/ Aton Pharma	timolol maleate	0.25% - unit dose; 0.5% - unit dose
Timoptic-XE/Aton Pharma	timolol maleate	0.25% - 2.5mL, 5mL; 0.5% - 2.5mL, 5mL
Prostaglandin Analogs Lumigan/Allergan	bimatoprost	0.01% - 2.5mL, 5mL, 7.5mL
Rescula/Sucampo	unoprostone	0.15% - 2.5mL, 5mL
Travatan Z/Alcon	travoprost	0.004% - 2.5mL, 5mL
Generic	latanoprost	0.005% - 2.5mL
Zioptan/Merck	Tafluprost	2.5mL

Topical Glaucoma Treatments

BRAND NAME/ MNFR	GENERIC NAME	CONCENTRATION/ BOTTLE SIZE
Alpha Agonists Generic	brimonidine	0.1%, 0.15% - 5mL, 10mL, 15mL
Alphagan P/Allergan	brimonidine	0.1%, 0.15% - 5mL, 10mL, 15mL
Iopidine/Alcon	apraclonidine	0.5% - 5mL, 10mL; 1% - unit dose
Carbonic Anhydrase Inhibitors Azopt/Alcon	brinzolamide	1% - 5mL, 10mL, 15mL
Trusopt/Merck	dorzolamide	2% - 5mL, 10mL
Combination Glaucoma Medications Combigan/Allergan	brimonidine/timolol	0.2%/0.5% - 5mL, 10mL
Simbrinza/Alcon	Brinzolamide/brimonidine	1%/0.2% - 8 mL
Cosopt PF/Merck Generic	dorzolamide/timolol	2%/0.5% - 5mL, 10mL

Selecting the Primary Medication
Open Angle Glaucoma

- Base the decision on:
  - PG usually the first medication selected
  - Stage of disease
    - driver for choosing initial therapy
  - Baseline IOPs
  - General health of patient
  - Insurance coverage
  - Systemic medications

Select Target Pressure

- Think in terms of Per Cent Reduction from highest IOP reading
- Greater the damage, lower the IOP needs to be
- Consider How bad is the glaucoma?
  - How long did it take to get that bad?
- What is the life expectancy of the patient?
- Trend is for lower target IOPs
  - sustained reduction

Target Pressures

- Setting the target IOP, consider highest IOP
  - IOP in 40 with some cupping, asymmetry and early field loss
    - IOP in low 20s may work
  - Same amount of damage but presenting IOP of 20
    - need to be more aggressive

Modifying the Medical Regimen Lack of Control

- IOP too high
  - Reverse Monocular Trial
- IOP Variability
- Optic Nerve Progression
- Visual Field Loss
- Adding a medication
  - medications vs. laser vs. filter surgery
  - add medication vs. increase dosage or concentration

Risk Factors for the Progression of Glaucoma

Risk Factors
Older age[1-3]
Higher IOP (baseline)[2]
Higher IOP (over follow-up)[2]
IOP fluctuation[4]
VF status at baseline[2]
Race (nonwhite)[3,5]
Disc hemorrhage[2,5]
Pseudoexfoliation[2]

When do you Add or Switch a Medication

- Tendency is to do nothing
- Tolerance develops to some medications
    - Beta Blockers, Alpha Agonists
- Is the angle getting narrow ?
  - Perform gonioscopy
  - Person can develop forms of glaucoma

Managing Glaucoma

- Initial medication
  - Prostaglandin
- Second medication
  - Topical CAI or Beta Blocker or Alpha agonist
  - Or switch to different prostaglandin
- Third medication or Modality-
  - Fixed Combination
  - Try to not exceed two bottles
- Fourth medication or modality
  - SLT
- Fifth modality- Surgery

When is surgery indicated?

- Poor control
  - progression noted in optic nerve or v. fields
  - account for variability on visual fields
    - repeat test to confirm change
- IOP above target pressure
  - exhausted several or all medical options
  - Account for IOP variability
- Medication side effects
- Poor compliance

Surgical Options

- Laser trabeculoplasty
  - Argon, Selective
- Filter surgery (trabeculectomy)
  - With anti-fibroblastic agents
- Setons and valves
  - Molteno, Ahmed
- New surgical procedures such as MIGS
  - Canaloplasty, Express implant, Trabectome, iStent