Evidence-Based Medicine in Evaluation of the Retinal Nerve Fiber Layer

An Essay

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Abstract

Evidence-based medicine (EBM) is "the meticulous, explicit and judicious use of current best evidence making decisions about the care of the individual patient. RNFL can be evaluated structurally and functionally. This study will review current literature on diagnostic modalities available for evaluation of retinal nerve fiber layer with emphasis on the best evidence available in the literature to support their use in clinical practice.

Keywords: Evidence-based medicine, retinal nerve fiber layer, confocal scanning laser ophthalmoscopy, optical coherence tomography, scanning laser polarimetry, standard automated perimetry, frequency-doubling technology perimetry, microperimetry.

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Table of Abbreviations

Abbreviation	Meaning
AION	Anterior Ischemic Optic Neuropathy
A-LHON	Atrophic Leber's hereditary optic neuropathy
Asb	Apostilbs
AUC	Area under the Curve
CCD	Charge-coupled device
C/D ratio	Cup-to-Disc area ratio
cd/m^2	Candelas per square meter
CON	Compressive optic neuropathy
CSLO	Confocal Scanning Laser Ophthalmoscopy
DD	The mean optic disc diameter
DDLS	Disc Damage Likelihood Scale
DLT	Differential light threshold
DM	The distance between the centre of the optic disc to the centre of the macula
DS	Dynamic strategy
EBM	Evidence-Based Medicine
EBO	Evidence-Based Ophthalmology
ECC	Enhanced corneal compensation
EGPS	European Glaucoma Prevention Study
ELM	External Limiting Membrane
EMGT	Early Manifest Glaucoma Trial
ERG	Electroretinogram
F	Discriminant Function
FDT	Frequency-Doubling Technology
FT	Full Threshold
FVEP	Flash Visual Evoked Potential
GCL	Ganglion cell layer
GDx	Scanning Laser Polarimetry
GDx VCC	Scanning Laser Polarimetry with variable corneal compensation
GPA	Guided progression analysis
GPS	Glaucoma Probability Score
HFA	Humphrey Visual Field Analyzer
HRP	High-Pass Resolution Perimetry
HRT	Heidelberg Retinal Tomography
ILM	Internal limiting membrane
INL	Inner nuclear layer
IPL	Inner plexiform layer
LHON	Leber's hereditary optic neuropathy
LVS	Low vision strategy
M-cell	Magnocellular retinal ganglion cell
MRA	Moorfields Regression Analysis
MRH	Mean Retinal Height

MRI	Magnetic Resonance Imaging
MS	Multiple Sclerosis
NAION	Nonarteritic anterior ischemic optic neuropathy
NFL	Nerve fiber layer
NS	Normal strategy
OCT	Optical Coherence Tomography
OHTS	Ocular Hypertension Treatment Study
ODD	Optic disc drusen
ONH	Optic nerve head
ONHD	Optic nerve head drusen
ONL	Outer nuclear layer
OPL	Outer plexiform layer
PCL	Photoreceptor Cell Layer
PVEP	Pattern Visual Evoked Potential
RGCL	Retinal Ganglion Cell Layer
RNFL	Retinal nerve fiber layer
ROC	Receiver Operating Characteristic
RPE	Retinal Pigment Epithelium
SAP	Standard Automated Perimetry
SD-OCT	Spectral Domain Optical Coherence Tomography
SITA	Swedish interactive thresholding algorithm
SLO	Scanning Laser Ophthalmoscope
SLP	Scanning Laser Polarimetry
SWAP	Short-wavelength Automated Perimetry
SWAP-FT	Short-wavelength Automated Perimetry Full Threshold
TCA	Topographic Change Analysis
TD-OCT	Time Domain Optical Coherence Tomography
TOP	Tendency Oriented Perimetry
UHR	Ultrahigh-resolution
VECPs	Visual Evoked Cortical Potentials
VEP	Visual Evoked Potential
VERs	Visual Evoked Response
ZEST	The zippy estimation of sequential testing
1-LT	One-level-test
2-LT	Two-level-testing
3-D	Three-Dimensional

Introduction to Evidence-Based Medicine:

The practice of medicine will always be a combination of science and art. We learn the artistic aspects from our teachers and our own experience. The scientific parts of medicine involve using evidence that has been gathered through the careful observations of others in the course of clinical research. Physicians have always attempted to use the best available medical knowledge to make decisions about their patients. During the early part of the twentieth century, the best available knowledge mainly consisted of techniques and approaches that had been passed on from other physicians. These techniques and approaches were rarely judged for effectiveness in a careful and systematic way. A movement toward improving the quality of medical practice with well-designed clinical trials began in the 1970s to 1980s.[1]

Evidence-based medicine (EBM) requires the integration of the best research evidence with our clinical expertise and our patient's unique values and circumstances.

- By **best research evidence** we mean valid and clinically relevant research, often from the basic sciences of medicine, but especially from patient-centered clinical research into the accuracy of diagnostic tests (including the clinical examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens. New evidence from clinical research both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones that are more accurate, more effective and safer. [2]
- By **clinical expertise** we mean the ability to use our clinical skills and past experience to rapidly identify each patient's unique health state and diagnosis, their individual risks and benefits of potential interventions, and their personal circumstances and expectation.[2]
- By **patient values** we mean the unique preferences, concerns and expectations each patient brings to a clinical encounter and which must be integrated into clinical decisions if they are to serve the patient. [2]
- By **patient circumstances** we mean their individual clinical state and the clinical setting.[2]

Importance of EBM:

The rapid spread of EBM has arisen from four realizations and is made possible by five recent developments. The **realizations**, attested to by ever-increasing numbers of clinicians, are:

1. Our daily need for valid information about diagnosis, prognosis, therapy, and prevention (up to five times per inpatient [3] and twice for every three outpatients).[4]
2. The inadequacy of traditional sources for this information because they are out of date (textbooks [5]), frequently wrong (experts [6]), ineffective (didactic continuing medical education [7]), or too great in their volume and too variable in their validity for practical clinical use (medical journals [8]).
3. The disparity between our diagnostic skills and clinical judgment, which increase with experience, and our up-to-date knowledge [9] and clinical performance[10], which decline.
4. Our inability to afford more than a few seconds per patient for finding and assimilating this evidence[11] or to set aside more than half an hour per week for general reading and study[12].

Until recently, these problems were great for full-time clinicians. However, five **developments** have permitted a turnaround in this state of interaction:

1. The development of strategies for efficiently searching and appraising evidence (for its validity and relevance).
2. The creation of systematic reviews of the effects of health care.
3. The creation of evidence-based journals of secondary publication (which publish the 2% of clinical articles that are both valid and of immediate clinical use) and of evidence-based summery services such as Clinical Evidence.
4. The creation of information systems for bringing the foregoing to us in seconds.
5. The identification and application of effective strategies for lifelong learning and for improving our clinical performance.[11]

Practice of EBM:

The Full-blown practice of EBM comprises five steps:

- **Step 1**: converting the need for information (about prevention, diagnosis, prognosis, therapy, causation, etc.) into an answerable question[13].

  Studies of information-seeking habits of physicians have shown that when asked, physicians reported that their practice generated about 2 questions for every 3 patients. Only 30% of physicians' information needs were met during the patient visit, usually by a colleague. Reasons for not using printed resources included office textbook collections too old, lack of knowledge of appropriate resources, and lack of time to find the needed information. However, studies have also shown that when clinicians have access to information, it changes their patient care management decisions[14].

  In 1998, Dr. David Sackett, using an "evidence cart" on rounds, reported that of 71 information searches to answer clinical questions, 37 (52%) confirmed the management decision, but 18 (25%) lead to a new therapy or diagnostic test and 16 (23%) corrected a previous plan[11].

- **Step 2***:* detecting the best evidence with which to answer that question.[15] When actually observed, investigators found that physicians had about 5 questions for each patient. 52% of these questions could be answered by the medical record or hospital information system. 25% could have been answered by published information resources such as textbooks or MEDLINE.[16]

- **Step 3**: critically appraising that evidence for its validity (closeness to the truth), impact (size of the effect), and applicability (usefulness in our clinical practice).[17]
- **Step 4**: integrating the critical appraisal with our clinical expertise and with our patient's unique biology, values, and circumstances.[18]
- **Step 5**: evaluating our effectiveness "doing the right thing" and efficiency "doing the thing right" in executing steps 1-4 and seeking ways to improve them both for next time.[19]

Evidence-Based Medicine Issues[20]

Opponents	Proponents
EBM is "old hat". Clinicians have been using the literature to guide their decisions for a long time. The label is new.	The new focus on EBM "formalizes" that "old hat" process and filters the literature so that decisions are made based on "strong" evidence.
EBM is "cook book medicine". It suggests that decisions are based solely on the evidence, downplaying sound clinical judgment.	EBM should be one part of the process. Decisions must be blended with individual clinical expertise, patient preferences & when available good evidence.
EBM is the mindless application of population studies to the treatment of the individual. It takes the results of studies of large groups of people and tries to apply them to individuals who may have unique circumstances or characteristics, not found in the study groups.	The last step in EBM process is to decide whether or not the information and results are applicable to your patient and to discuss the results with the patient.
There is often great difficulty in getting access to the evidence and in conducting effective searches to identify the best evidence.	Librarians can help identify the best resources and teach clinicians effective searching skills.

Thus, we can conclude that evidence-based medicine (EBM) is a medical mode that is completely different from traditional experience-based medicine. The core of EBM is that decision-making during clinical practice must be based on objective research results. With the rapid development of modern ophthalmology, some former viewpoints according to experience-based medicine face challenges. Evidence-based ophthalmology (EBO) is crucial as one challenge for ophthalmologists entering the 21st century will be to make clinical decisions based on valid information or evidence rather than suspicion, hearsay, or peer practice.[21]

Levels of EBM:

The evidence levels recommended by the US Preventive Services Task Force, given to provide a framework for evaluating the current peer-reviewed literature (through October 2007) on both measures of structure and function in the diagnosis and follow-up of glaucoma:

Level I: (Interventional) Evidence obtained from at least one properly done, well-designed randomized controlled trial or meta-analysis of high-quality randomized controlled trials;

Level I: (Observational) Evidence obtained from well-done, population-based prevalence or incidence studies;

Level II: (Interventional) Evidence obtained from well-done, non-randomized comparative trials or well-done, systematic literature reviews summarizing primarily level II publications;

Level II: (Observational) Evidence obtained from high-quality, case-control and cohort studies; and

Level III: (Interventional or Observational) Evidence obtained from non-comparative case series, case reports, and expert or consensus opinion.[22]

Anatomy of the Retinal Nerve fiber Layer:

The human retina is composed of 10 anatomically distinct layers: (1) retinal pigment epithelial cell layer (RPE), (2) photoreceptor cell layer (rods and cones), (3) external limiting membrane, (4) outer nuclear layer, (5) outer plexiform layer, (6) inner nuclear layer, (7) inner plexiform layer, (8) ganglion cell layer, (9) nerve fiber layer, and (10) internal limiting membrane[23] (Figure1).

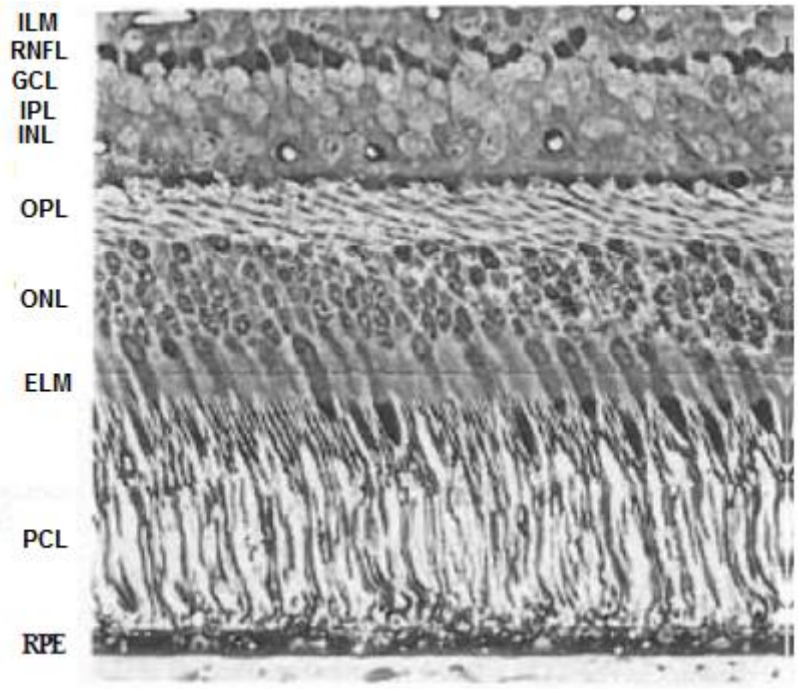

Figure (1): Histologic architecture of the primate retina. RPE, Retinal pigment epithelial cell layer; PCL, photoreceptor cell layer; ELM, external limiting membrane; ONL, outer nuclear layer; OPL, outer plexiform layer; INL, inner nuclear layer; IPL, inner plexiform layer; GCL, ganglion cell layer; RNFL, retinal nerve fiber layer; ILM, internal limiting membrane. (Quoted from Yanoff M and Duker JS (2004)) [23]

The nerve fiber layer is the innermost layer of the retina and is visible to an examiner using direct or indirect ophthalmoscopy. This layer is composed of ganglion cell axons, neuroglia, and astrocytes. The axons are gathered together in bundles surrounded by neuroglia.[24]

Six studies have, to date, quantified the thickness of the RNFL histologically in primate and human eyes[25]. While each used a different approach, the cumulative data define several key characteristics of the RNFL in