Commentary: Spectral domain optical coherence tomography parameters in pre-perimetric glaucoma

Glaucoma is an irreversible optic neuropathy characterized by increased cupping, thinning of circumpapillary retinal nerve fiber layer (cpRNFL), and the neuroretinal rim, and loss of retinal ganglion cells.[1] It is usually asymptomatic in the initial stages, and structural changes precede the development of repeatable visual field defects.[2] Therefore, early detection and treatment of the disease maybe paramount to amelioration of the prognosis.

With the advent of Spectral Domain Optical Coherence Tomography (SD-OCT), the ability to detect early glaucoma have significantly improved using advanced ONH, RNFL and macular imaging.[3] RNFL thickness is the most commonly used diagnostic parameter followed by parameters in the macular region and the ONH.[3] RNFL thickness measurements have good reproducibility, a proven structural and functional relationship and can be used to detect glaucoma progression. However, RNFL thickness values are not interchangeable between different machines. The ability to detect changes associated with glaucoma is quantified as an area under the receiver operating characteristic curve (AUROC) value. The receiver operating characteristic curve (ROC) is created by plotting the true positive rate (i.e., Sensitivity) against the false-positive rate (i.e., specificity) at various threshold settings. An excellent test generally has AUROC values between 0.90 and 1, a good test between 0.80 and 0.90, a fair test between 0.70 and 0.80, and a poor test between 0.60 and 0.70. However, GCIPL, RNFL, and optic disc parameters showed a similar ability to detect glaucoma and the combined predictive formula improved the glaucoma detection compared to isolated parameters.[3]

Macular imaging of the retinal ganglion cells (RGCs) provides a direct way to detect glaucoma damage as the RGCs have less intersubject anatomic variability and owing to the presence of a large number of RGCs in the macular area, aids in early detection.

Most of the studies compared glaucoma in the advanced stages with repeatable visual field defects and healthy controls. To assess the potential of imaging devices as ancillary diagnostic tests, however, one needs to evaluate their performance in the presence of diagnostic uncertainty. Healthy eyes have unusual anatomic features that confuse currently available diagnostic software. Myopia, a classic example of that, is associated with larger optic disc and high variability in RNFL thickness, is more likely to simulate a clinical scenario of diagnostic uncertainty.[4,5] Rao *et al*. reported decreased ability of SD-OCT parameters to detect glaucoma when evaluated against a clinically relevant control group that had suspicious appearance of the optic disc.[6]

Lisboa *et al*.[7] included patients with suspicious discs and no repeatable visual field defects for studying the SD-OCT parameters. Cases and controls were selected based on the documented evidence of progressive glaucomatous change in the optic disc before the imaging sessions, graded as pre-perimetric glaucoma. They found that the average RNFL thickness, Vertical Cup Disc Ratio and GCC average thickness had the largest AUROCs in the RNFL, ONH and macular parameters respectively. However, RNFL assessment performed significantly better than ONH and macular assessment in detecting pre-perimetric discs.

Rao *et al*. studied the ability of SD-OCT to differentiate pre-perimetric glaucomatous disc from large physiological optic disc cups. Pre-perimetric glaucoma was diagnosed as the presence of glaucomatous optic neuropathy on masked evaluation of optic disc photographs by two glaucoma experts and normal visual field. All parameters were significantly different between the two groups with the highest AUC on ONH, RNFL and GCC parameters being vertical cup disc ratio, inferior quadrant RNFL thickness, and inferior quadrant GCC thickness, respectively.[8]

The authors similarly compared SD-OCT parameters in disc suspects, which were selected based on a fixed selection criteria seen on optic disc photos. However, the authors did not state the selection criteria of pre-perimetric glaucomatous discs. Also, they only did a qualitative analysis on OCT which may not be reproducible unlike other studies in literature.[9]

Most importantly, there is no standard accepted definition of preperimetric glaucoma itself, making diagnostic evaluations arbitrary.

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Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_2960_20

Cite this article as: Lakra S, Angmo D. Commentary: Spectral domain optical coherence tomography parameters in pre-perimetric glaucoma. Indian J Ophthalmol 2021;69:610-1.