Original Article

Clinical, ultrasonographic and optical coherence tomography correlation of optic nerve head cupping in glaucoma patients

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Purpose: To ascertain if ultrasound (USG) B-scan examination of the optic nerve head (ONH) can be a useful tool to diagnose and quantify glaucomatous cupping. **Methods:** A cross-sectional observational study of 48 eyes of 48 patients with clear ocular media and cup-disc ratio of (CDR) ≥0.6 were included. The disc was studied by + 90D examination, USG B-scan and ONH Optical coherence tomography (OCT) by three masked observers. Observer-1 assessed the clinical CDR, observer-2recordedopticcup diameter on USG B-scan and observer-3performed ONH OCT to note the software computed average CDR. Measurements of cupping obtained by these 3 methods were compared and their relative strengths determined. The interdependency between variables was further studied using regression analysis. **Results:** Clinically assessed disc ratios of 0.6, 0.7, 0.8, 0.9, and total corresponded to USG cup measures of 1.02 ± 0.11 mm, 1.23 ± 0.14 mm, 1.35 ± 0.072 mm, 1.45 ± 0.084 mm, 1.75 ± 0.15 mm and OCT average CDR of 0.62 ± 0.087, 0.68 ± 0.060, 0.75 ± 0.078, 0.81 ± 0.036, 0.89 ± 0.038, respectively. There was an excellent correlation between the three arms, with Pearson's co-efficient (r) of 0.87, $P < 0.001$ between clinical and USG cupping; r = 0.89, $P < 0.001$ between clinical and OCT cupping; and r = 0.88, $P < 0.001$ between USG and OCT cupping. A relation of y = 1.64x + 0.03 was obtained between them, where y stands for USG cup diameter and x stands for the observed clinical CDR. **Conclusion:** Ultrasonographic measurement of optic cup diameter corresponds well to clinical ONH cupping. Therefore, it can reliably be used in quantifying ONH cupping in cases of media opacities which preclude optic disc visualization.

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In routine clinical practice, before planning any form of surgical intervention for a patient, the visual prognosis needs to be clearly explained. In the present scenario where cataract surgeries are being performed with very least margins of errors, the expectation of visual gain following surgery remains high. If advanced glaucoma remained hidden behind an opaque media and was unrealized prior to surgery, the aftermath may be disappointing.[1]

In challenging situations where direct visualization of the optic nerve head (ONH) is not possible, measurement of intraocular pressure and pupillary reactions are taken as a surrogate for glaucoma.[2] However, conditions like ocular hypertension and normal tension glaucoma may make this fallacious.[3,4] Hence, some form of ONH evaluation is crucial. Patients with media opacity routinely undergo ultrasound (USG) B-scan for posterior segment evaluation, excavation when noted in the optic disc region, the suspicion of glaucoma needs to be deciphered; however, this is subjective, with significant inter-observer variation, and the extent of cupping cannot always be assessed. Hence, this study compared clinically visible glaucomatous cupping to ONH dimensions on USG B-scan and automated cup-disc ratio (CDR) on optic coherence tomography (OCT) for an objective evaluation.

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Methods

Consecutive known glaucoma patients at the glaucoma services of a tertiary eye care center between January to July 2017 were screened. Patient aged >18 years having clear ocular media that allowed direct visualization of the disc were evaluated (n = 75). Those with normal sized ONH and clinical CDR ≥ 0.6 consistent with features of glaucomatous optic neuropathy (neuroretinal rim thinning, retinal nerve fiber layer defects, nasalization, and bayonetting of large vessels, baring of circumlinear vessels and disc hemorrhages) were recruited in the study (n = 50) (examined by a glaucomatologist – observer 1). Patients with small/large sized discs (n = 15), tilted discs (n = 3), myopic discs (n = 3), physiological cupping (n = 2), any other optic nerve diseases (n = 1), and those not willing to participate in the study (n = 1) were excluded. An informed consent was taken from each patient and the study adhered to basic tenets of the declaration of Helsinki.

Observer 1 identified and examined the ONH status of each patient by +90 D biomicroscopy and stratified them into five

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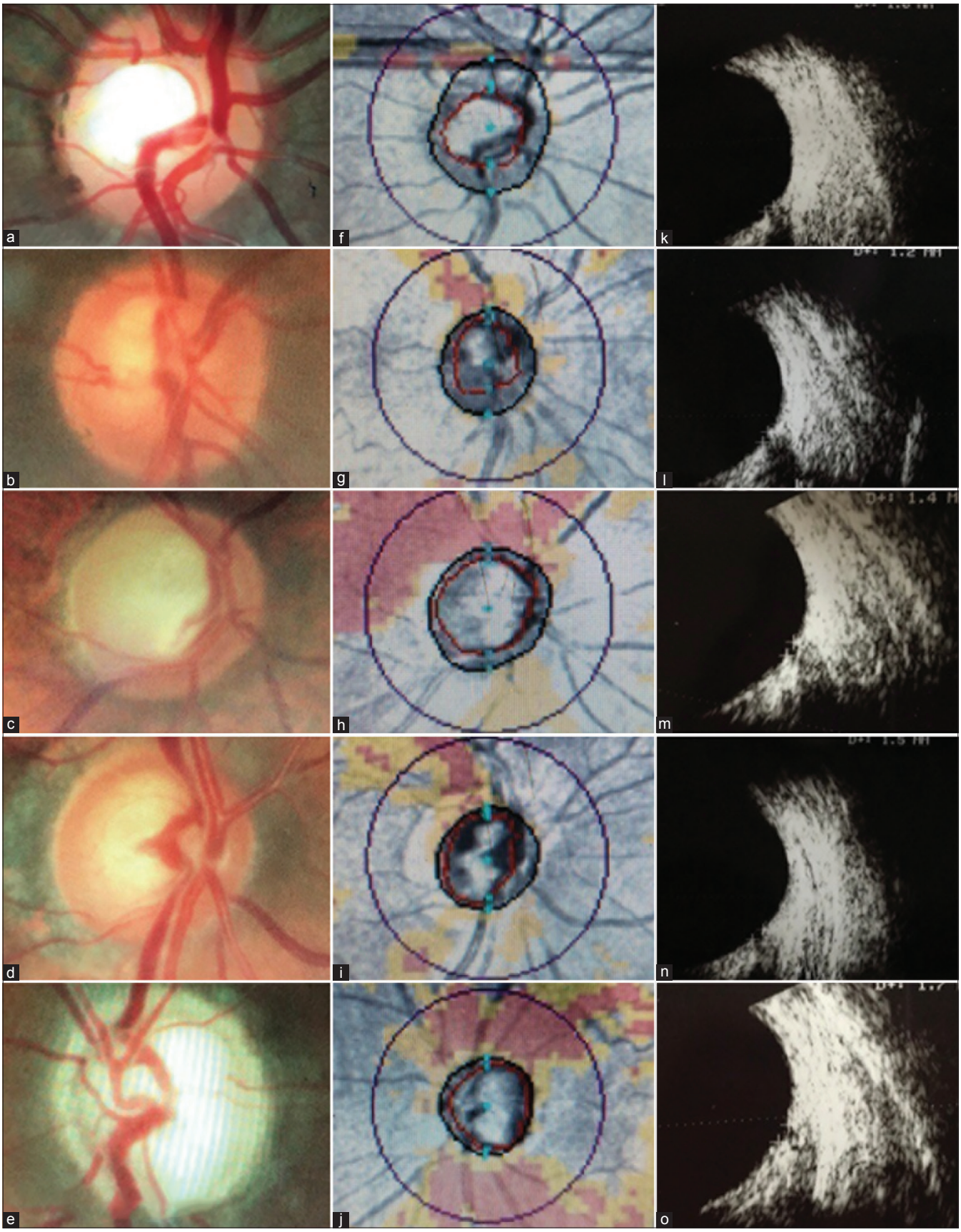


Figure 1: (a-e) Clinically documented optic disc cupping from 0.6 to total cupping A (0.6), B (0.7), C (0.8), D (0.9), E (total). (f-j) Respective OCT documented cupping from 0.6 to total. (k-o) Ultrasonographically quantified cupping from 0.6 to total. The amount of excavation along the optic nerve head is quantified in millimetres and the same has been depicted in the right upper corner of each ultrasound picture

groups based on the clinical CDR as group 1: 0.6, group 2: 0.7, group 3: 0.8, group 4: 0.9, and group 5: total cupping. Each group consisted of ten patients; one eye of each patient was included, summing up to a total of 50 eyes of 50 patients. [Fig. 1a-e]

A second masked observer did USG B-scan (E-Z Scan AB5500+, Sonomed Escalon, New York, USA) (10 MHz, 80 dB gain) for each of them to assess the ultrasonographic ONH cupping. The patient was explained about the procedure and made to lie down comfortably on a couch in supine position. Over the closed eyelids, after applying a coupling agent, the probe was placed along the lateral longitudinal plane to focus on the optic nerve head. Once an adequate focus is obtained, the image was frozen and the distance between the edges of the optic nerve head excavation was measured using inbuilt calipers in millimeter scale. This was noted as the ultrasonographic ONH cup diameter.

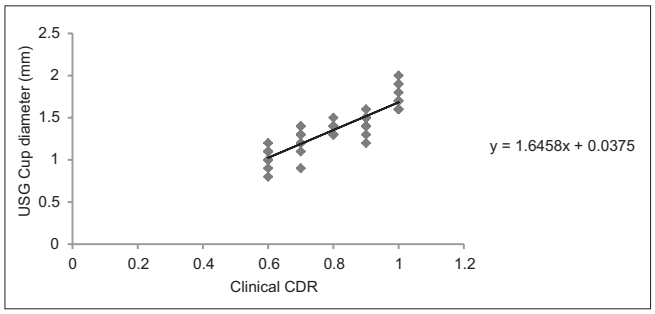
A third masked observer performed a posterior segment OCT in ONH-RNFL module (Cirrus HD OCT, Carl Zeiss Meditec, Dublin, CA) and recorded the software computed average CDR.

Statistical analysis

Statistical analysis was done using Stata 12.1 software. Categorical values were summarized as frequency (%) and quantitative values were summarized as mean ± standard deviation, or median (range) if not normally distributed. Correlation between different parameters was studied by Pearson correlation test. A *P* value of < 0.05 was considered statistically significant. The predictability of clinical CDR on USG was further studied using regression analysis.

Results

Of the 50 eyes, two eyes had poor quality OCT scans on final analysis and were excluded from the study. Thus, group 1 consisted of 10 eyes, group 2 of 10 eyes, group 3 of 9 eyes, group 4 of 10 eyes, and group 5 of 9 eyes. The mean age of patients studied was 51.33 ± 15.46 years (range, 40–74), and 26 (54%) were males. The mean OCT measured ONH vertical CDR for each group was 0.62 ± 0.087, 0.68 ± 0.060,0.75 ± 0.078, 0.81 ± 0.036, 0.89 ± 0.038 in group 1 to 5, respectively. [Fig. 1f-j] Similarly, the mean USG measured ONH cup diameter was 1.02 ± 0.11 mm, 1.23 ± 0.14 mm, 1.35 ± 0.072 mm, 1.45 ± 0.084 mm and 1.75 ± 0.15 mm for groups 1-5. [Fig. 1k-o]



Graph 1: Graph showing correlation between Clinical cup-disc ratio (CDR) and ultrasound (USG) Cup diameter. Cup-disc ratio (CDR), Ultrasonography (USG). y: Predicted USG cup diameter, x: Clinical CDR

Table 1: Clinical correlation of optic disc cupping with ultrasonography (USG) and optical coherence tomography (OCT)

Clinical CDR	USG ONH cup diameter	OCT CDR
0.6 (*n*=10)	1.02 mm±0.11	0.62±0.087
0.7 (*n*=10)	1.23 mm±0.14	0.68±0.060
0.8 (*n*=9)	1.35 mm±0.072	0.75±0.078
0.9 (*n*=10)	1.45 mm±0.084	0.81±0.036
Total (*n*=9)	1.75 mm±0.15	0.89±0.038

CDR=Cup-disc ratio, ONH=Optic nerve head

On correlating clinical CDR, ONH cup diameter and OCT CDR of each group, all three within each group showed an excellent positive correlation. The Pearson's correlation co-efficient (r) was 0.87, $P < 0.001$ between clinical and USG cupping; r = 0.89, $P < 0.001$ between clinical and OCT cupping; and r = 0.88, $P < 0.001$ between USG and OCT cupping. On a regression model, a relation of y = 1.64x + 0.03 was obtained, where y stands for estimated USG cup diameter, and x stands for the observed clinical CDR [Graph 1 and Table 1].

Discussion

Glaucomatous optic neuropathy is characterized by selective loss of neuroretinal rim, which leads to increase in cup size, better presented clinically as increased cup-disc ratio. Though focal notching can occur, it is the increase in vertical CDR that is more often seen in clinical practice.[5-7] Optic disc cupping can also be seen is some neuro-ophthalmic disorders, however, rim pallor would be disproportionate to the amount of cupping.[8]

An accurate assessment of optic nerve head is crucial for diagnosis and follow-up of glaucoma patients, especially when perimetry cannot be performed. Newer diagnostic modalities such as optical coherence tomography and Heidelberg retinal tomography (HRT) aid in objective assessment of disc morphology and detection of structural progression.[9,10] These investigations require a clear ocular media and sometimes pupillary dilation, putting patients with media opacities, and non-dilating pupils at disadvantage. An ultrasound B-scan is almost always done for them to evaluate the posterior segment, and minimal extra effort to measure the optic cup diameter can help in detecting glaucoma. On USG, optic nerve is a regular tubular structure with low reflectivity, surrounded by a highly reflective peri-neural sheath and heterogeneous orbital fat, making it a good candidate for echo graphic imaging.[11]

This study found excellent positive correlation between USG cup diameter and CDR assessed by + 90D and OCT in cases with ≥ 0.6 glaucomatous cupping. Their trend showed a steady change such that a statistically derived formula could predict clinical CDR from the USG measured cup diameter values. This ability to equate or predict the clinical and USG cupping by numerical values is being put forth by us for the first time in literature, to the best of our knowledge. In this study, we directly saw the clinical cupping, therefore, the formula was put forth to derive the USG cupping. But in cases of opaque media, the formula can be simply rearranged such that the USG measurements are entered and the clinical CDR be calculated, that is, x = (y-0.03)/1.64. For example, if the measured cup diameter (distance between the excavation margins) was 1.2 mm, then (1.2-0.03)/1.64 = 0.7 clinical cupping, provided it is a normal sized disc.

Few studies in literature have elucidated the ability of modern B- scan ultrasonography to detect optic disc cupping using parameters like vertical optic cup diameter, horizontal optic

cup diameter and retro-bulbar optic nerve diameter.[12,13] They demonstrated a strong correlation between the ultrasonographic measurements of optic disc cups and the cup: disc ratio compared with imaging techniques like OCT and HRT. Cohen *et al*. in 1976 reported ultrasonographic detection of glaucomatous cups with CDR >0.7, however, it was a small series of only 6 eyes, and importantly, they could not quantify it.[12] Winder S, *et al*. suggested that high-resolution B- scan ultrasound can detect vertical optic disc cups of 0.5 mm or larger.[13] They also showed a good correlation between ultrasonographic measurements of optic disc cups and clinical vertical cup diameters and cup: disc ratios. However, being unable to assess the disc size, large cups in a small disc can be deceptively labeled as small cups. Also, the study did not find any correlation between optic disc size and retrobulbar optic nerve size. Darnley-Fisch *et al*. could detect optic disc cups with CDR as low as 0.3.[14] Nadir Ali *et al*. measured optic disc cups as small as 0.2.[10] The latter study revealed no statistically significant difference between the optic cup diameters measured by sonography and fundus photography even for small cups, and proposed USG as a viable alternative in eyes with opaque media. In addition, they showed that it is possible to combine the sonographic measurement of the optic cup diameter from the eye with opaque media and the fundus photographic measurement of optic disc diameter from the fellow ''clear'' eye to calculate the cup: disc ratio in a patient with unilateral ocular media opacity.

The resolution of ultrasonography has evolved with time, and now it has become an indispensable tool for the assessment of various posterior segment diseases.[15,16] Thus, its utility in the evaluation of glaucoma cases cannot be underestimated. The utility of ultrasound is high in countries like ours where patients with advanced cataracts or anterior segment opacities are so common, this tool is often necessary to decipher the posterior segment pathology.

However, certain limitations should be kept in mind while interpreting ultrasonography imaging findings. B-scan can only detect the relative size of the optic disc cup. Thus, quoting an USG cup: disc ratio would be erroneous since the edges of the disc cannot be discerned by ultrasonography.[17] A number of studies associating structural optic disc measurements and practical disability have failed to demonstrate CDR as a reliable predictor of field loss.[18-20] Hence, despite a large cup detected on USG, some patients may still have reasonable visual potential. Also, physiological cupping may mimic glaucomatous cupping on USG. Though glaucomatous optic neuropathy usually presents with an increase in overall CDR, cases of focal notching do occur and may be underestimated or missed on USG. The main limitations of our study include a small sample size, a cross-sectional design and recruitment of patients with only ≥0.6 cupping. If the patients could be followed up to document an increase in USG cup diameter in due course of structural progression, it could be more meaningful.

Conclusion

To conclude, our study has shown an excellent positive correlation between clinical CDR assessed by a glaucomatologist, the ONH cup diameter measured by ultrasound B-scan and vertical CDR measured by ONH-RNFL OCT. This study also provides some normative data of USG measured ONH cup diameters corresponding to clinical vertical CDR ≥0.6, and has derived a statistical formula to predict the former from the latter. Thus, in cases of media opacities, USG can be a useful tool to detect and quantify the extent of ONH cupping to aid in management and prognostication.

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Conflicts of interest

There are no conflicts of interest.

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