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Original Research Article

Comparison of visual fields and retinal nerve fiber layer thickness in assessing optic nerve head damage in patients with primary open-angle glaucoma

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ABSTRACT

Purpose: This study aims at evaluating the relationship between visual fields by HFA and retinal nerve fibre layer thickness and ONH parameters by OCT in assessing optic nerve head damage in patients with primary open-angle glaucoma.

Materials and Methods: A total of 87 glaucomatous eyes were included. All subjects underwent complete ophthalmic examination, gonioscopy, visual field examination by Humphrey's automated visual field analyzer and RNFL thickness and ONH parameters assessment by SD-OCT. Glaucomatous eyes were graded according to Hodapp, Parrish, and Anderson's classification. Quadrant wise RNFL thickness and average thickness were recorded. Statistical analysis was done using Epidemiological Information Package (EPI) version 7.2.

Results: Average and vertical CD ratio was found to be the most important ONH parameter to discriminate early from moderate glaucoma and for assessing progression from moderate to severe glaucoma. All ONH parameters except the disc area were significant. A significant correlation was detected between mean deviation, pattern standard deviation, and average RNFL thickness. Average RNFL thickness was the best parameter to discriminate early from moderate, and moderate from severe glaucoma. The sectoral RNFL thicknesses also showed a gradual decline and were statistically significant in all sectors in moderate and severe glaucoma and only in inferior and superior sectors in mild and moderate glaucoma.

Conclusion: In the present study, average RNFL thickness had a good diagnostic value in the diagnosis of glaucoma and for grading of glaucoma according to its severity. The structural changes on OCT correlated well with functional damage shown on visual fields.

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1. Introduction

Glaucoma is a chronic progressive optic neuropathy characterized by morphologic changes of cupping of the optic nerve head (ONH), changes in the retinal nerve fibre layer (RNFL) subsequently followed by characteristic visual field (VF) loss.¹ The final common pathologic event is retinal ganglion cell (RGC) death.² Primary open-angle glaucoma (POAG) is a chronic, bilateral disease in which there is acquired loss of optic nerve fibres, VF abnormalities

with an open anterior chamber angle, and raised intraocular pressure which is detrimental to the structural and functional integrity of ONH.³

Glaucoma is estimated to be the second most common cause of blindness all over the world. The number of POAG patients is estimated to be nearly 67 million worldwide, with only half of them diagnosed in developed countries.⁴ In developing countries the identification rate of known POAG cases is even lower. Glaucoma suspects are nearly 105 million as determined by the World Health Organization.⁵

Careful examination of the disk parameters including size, shape, neuroretinal rim shape and pallor; presence and

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location of splinter-shaped haemorrhages; occurrence, size, configuration, and location of parapapillary chorioretinal atrophy; and visibility of the RNFL are important in glaucoma cases. These observations can be documented in the form of photographs taken by a fundus camera.⁶ Visual field loss clinically correlates with RNFL loss and ONH damage. In the natural evolution of POAG, there is a loss of ganglion cells and their axons in the retina. A significant amount of ganglion cell death (25 to 30%) has to occur before any visual field defect is produced and thus here comes the concept of pre-perimetric glaucoma.⁷ Careful evaluation of the ONH and RNFL is crucial in glaucoma, not only for the diagnosis but also for providing information about the location and severity of visual field damage. OCT may be useful in glaucoma screening in the high-risk group.⁸

The purpose of the present study is to find the relationship between visual fields analysis by HFA and retinal nerve fibre layer thickness and ONH parameters by OCT in assessing optic nerve head damage in patients with primary open-angle glaucoma.

2. Materials and Methods

The present study is a hospital-based cross-sectional study conducted in the outpatient department of Ophthalmology, SVRRGGH between 2020 and 2021. A total of 50 patients diagnosed with primary open-angle glaucoma who were willing to participate were enrolled in the study. Patients with significant media opacities which can interfere with the clarity of fundus photographs, recording of the visual field and RNFL analysis by OCT and patients with other ocular diseases or retinal pathologies which can affect the RNFL thickness were excluded from the study.

This study was conducted in accordance with the declaration of Helsinki, and Institutional Ethics Committee approval was obtained prior to the study. All patients were informed about the study procedure and written consent was taken prior to their inclusion.

Data was collected in a Standardised proforma from all the patients who met the inclusion criteria. This included a detailed clinical and ophthalmic history, best-corrected visual acuity and complete anterior segment evaluation by slit-lamp biomicroscopy. Intraocular pressure was measured by Goldmann applanation tonometry and Gonioscopy was done by Zeiss 4 mirror Goniolens to assess the angle of the anterior chamber. Disc evaluation was done by direct ophthalmoscopy & slit-lamp biomicroscopy using a +90D lens. Visual field examination was performed by Humphrey's automated visual field analyzer type-II – 720 I series. A standard white on white perimetry with SITA strategy was performed using a 24-2 program for diagnosis and follow-up. The 10-2 program was used for cases with fixation threats. RNFL thickness and ONH parameters were assessed by Spectral-domain Optical

Coherence Tomography. All OCT scans were performed through a dilated pupil by a single examiner.

2.1. Statistical analysis

The data collected was recorded in a Master Chart. Data analysis was done using Epidemiological Information Package (EPI 2010) developed by the Centre for Disease Control, Atlanta. EPI version 7.2 was used to calculate range, percentages, means, standard deviations, and 'p' values. A p-value less than 0.05 was considered to be statistically significant.

3. Results

A total of 50 POAG patients were included in the study. Out of 100 eyes of 50 patients, 87 eyes were taken into the study. Of the 13 eyes which were excluded from the study, 7 eyes had hazy media, 1 patient had an empty socket, and 5 eyes had a low vision (only PL +). As VF and OCT could not be performed, these eyes were excluded from the study.

Among 87 eyes studied 46(53%) were right eyes and 41(47%) were left eyes. Age distribution among subjects was between 41-85yrs, with a mean age of 60.12 years and a standard deviation of 10.48years. The majority of the patients 25 (50%) were aged 60yrs and above, 9 patients (18%) belonged to the 40-49yrs age group and 16(32%) belonged to the 50-59yrs age group. Among 50 patients 28(56%) were males and 22(44%) were females.

3.1. Visual field defects by humphreys visual field analyser

Of the various field defects noted, biarcuate scotoma was seen in 26 eyes (29%) and was the most frequent field defect recorded as shown in Table 1.

Table 1: Distribution of visual field defects (n=75)

| Visual field Defect | No of Eyes (Percentage%) |
|---------------------------|--------------------------|
| Paracentral scotomas | 5 (5.74) |
| Superior arcuate scotoma | 18 (20.68) |
| Inferior arcuate scotoma | 15 (17.24) |
| Biaruate scotoma | 26 (29.88) |
| Temporal island of vision | 9 (10.34) |

All 87 eyes were divided into 3 groups mild, moderate & severe based on Hodapp, Parrish and Anderson classification. According to this classification eyes with MD < 6 dB on visual fields were classified as mild glaucoma, those with MD 6-12dB as moderate glaucoma and those eyes with MD >12 dB as severe glaucoma. According to this classification majority of the eyes, 60% belonged to the severe glaucoma group.(Table 2)

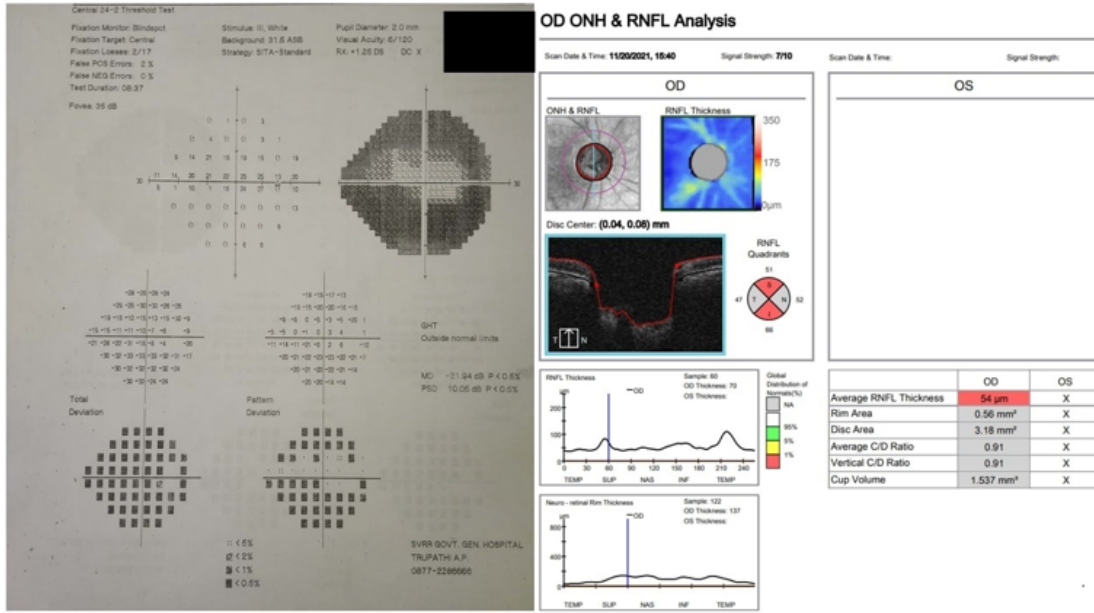


Fig. 1: Case no. 1 This was a 54-year-old male patient with 8-year history of glaucoma, with the following data upon examination. Visual fields show advanced glaucomatous field defects with corresponding OCT analysis

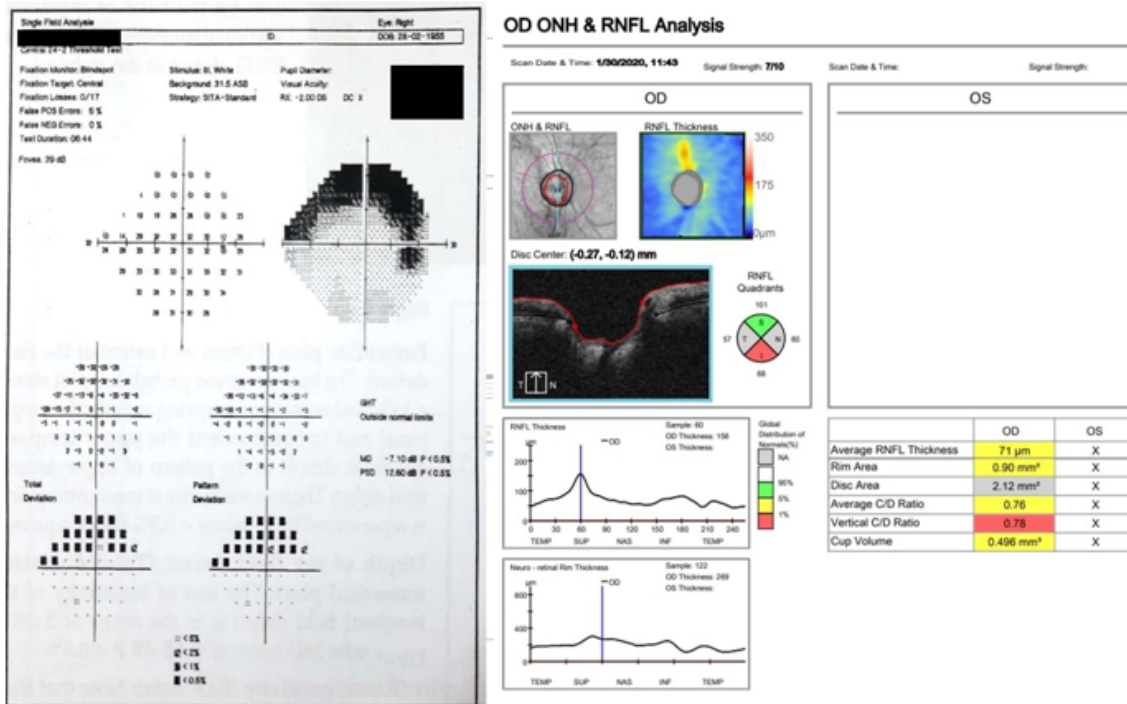


Fig. 2: This was a 49-year-old male patient with 5-year history of glaucoma, with the following data upon examination. Visual fields showing superior arcuate scotoma with corresponding OCT analysis showing thinning in the inferior quadrant

Table 2: Distribution of eyes based on Hodapp, Parrish and Anderson classification and their average mean deviation and standard pattern deviation

| Mean deviation | Severity of glaucoma | No of eyes (Percentage) | Average mean deviation (dB) | Average pattern standard deviation (decibel) |
|----------------|----------------------|-------------------------|-----------------------------|--|
| <6 Db | Mild glaucoma | 13 (14.94) | 4.54 ± 0.25 | 2.43 ± 1.35 |
| 6-12Db | Moderate glaucoma | 21 (24.13) | 10.48 ± 2.36 | 4.89 ± 2.55 |
| >12Db | Severe glaucoma | 53 (60.91) | 26.71 ± 12.63 | 7.88 ± 1.76 |

Table 3: ONH parameters of eyes divided based on the severity of glaucoma

| ONH Parameters | Mean ± SD | Mild Glaucoma | Moderate Glaucoma | Severe Glaucoma | Mild vs moderate p-value | Moderate vs severe p-value |
|-------------------------------|------------|---------------|-------------------|-----------------|--------------------------|----------------------------|
| Average CD ratio | 0.68±0.37 | 0.48±0.13 | 0.69±0.04 | 0.98±0.54 | 0.005 | 0.052 |
| Vertical CD ratio | 0.76±0.45 | 0.48±0.06 | 0.78±0.05 | 0.97±0.72 | 0.002 | 0.032 |
| Disc area (mm ²) | 2.25±0.16 | 2.12±0.56 | 2.46±0.17 | 2.36±0.34 | 0.305 | 0.703 |
| Rim area (mm ²) | 1.21±0.89 | 2.06±0.13 | 1.96±0.11 | 0.55±0.39 | 0.036 | 0.086 |
| Cup volume (mm ³) | 0.705±0.36 | 0.154±0.05 | 0.537±0.67 | 1.09±0.72 | 0.006 | 0.046 |

Table 4: RNFL thickness of eyes divided based on the severity of glaucoma

| RNFL Thickness (μm) | Mean ± SD All patients | Mild Glaucoma | Moderate Glaucoma | Severe Glaucoma | Mild vs moderate glaucoma (p-value) | Moderate vs severe (p-value) |
|---------------------|------------------------|---------------|-------------------|-----------------|-------------------------------------|------------------------------|
| Average | 79.06±13.51 | 100.34±6.76 | 82.9±10.66 | 64.71±9.47 | 0.00 | 0.001 |
| Inferior quadrant | 90.39±13.17 | 124±13.46 | 98±16.23 | 84.31±8.09 | 0.032 | 0.007 |
| Superior quadrant | 92.99±12.78 | 109±10.26 | 96.01±9.92 | 87.98±11.32 | 0.011 | 0.038 |
| Nasal quadrant | 73.14±17.80 | 75.45±5.66 | 70.5±10.7 | 66±9.10 | 0.339 | 0.075 |
| Temporal quadrant | 59.23±8.15 | 72±8.22 | 68.04±14.75 | 54.62±10.15 | 0.365 | 0.028 |

3.2. RNFL and optic nerve head analysis by OCT

As the severity of glaucoma increased average CD ratio, vertical CD ratio and cup volume showed a gradual increase which was statistically significant. The rim area showed a gradual decline between the groups and was also statistically significant. But, the change in disc area failed to show any statistical significance when compared between the groups. The study showed a direct relationship between severity of glaucoma (which is denoted by MD by VF) and average CD ratio, vertical CD ratio and cup volume. The severity of glaucoma was inversely related to the rim area in the study. (Table 3)

In assessing the change from mild to moderate glaucoma, average and vertical CD ratios (which were highly significant) can be considered as the most important ONH parameters and for assessing progression from moderate to severe glaucoma all the ONH parameters except disc area can be taken into consideration.

The average RNFL thickness was 79.06 ± 13.51 μm. The RNFL was found to be thickest in the superior sector with a mean thickness of 92.99 ± 12.78 μm and thinnest in the temporal sector with a mean thickness of 59.23 ± 8.15 μm. The ISNT rule was not obeyed in the study eyes.

3.3. Correlation between visual field analysis by HFA and RNFL thickness and ONH analysis by OCT

The average RNFL thickness showed a statistically significant decrease as the severity of glaucoma increased.(Table 4)

1. Between moderate and severe glaucoma, the thickness of sectoral RNFL decreased gradually in all sectors, which was statistically significant.
2. Between mild and moderate glaucoma, only the inferior and superior sectors of RNFL showed statistical significance.

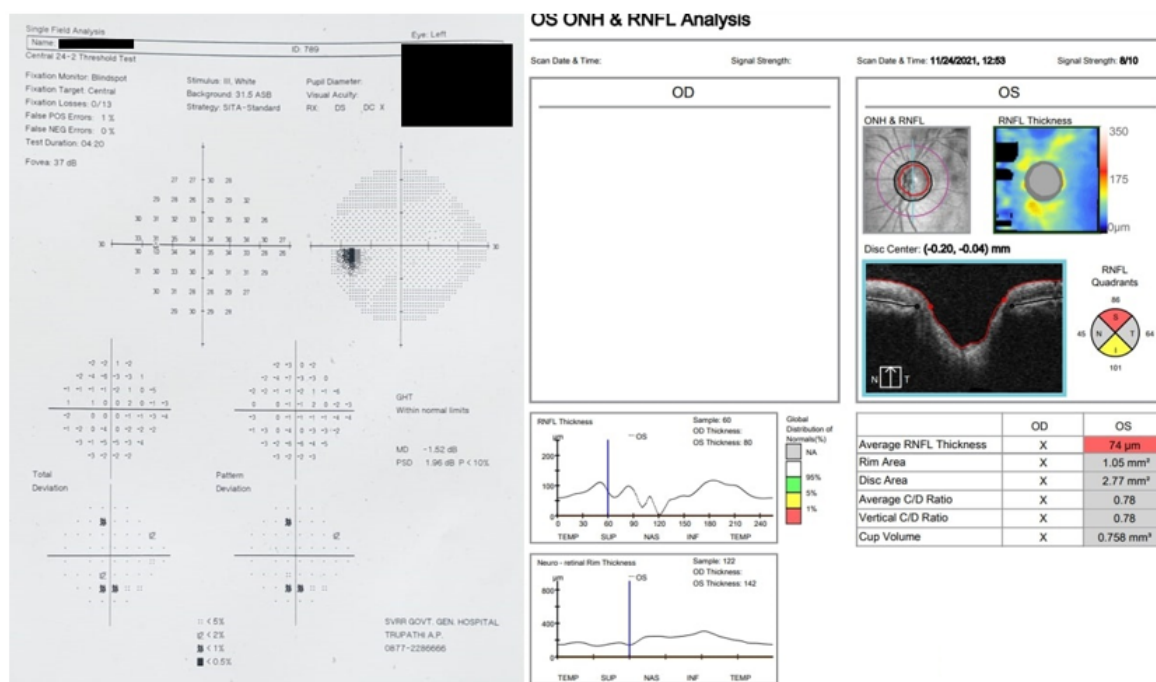


Fig. 3: Case no. 3 This was a 40-year-old male patient with 2-year history of glaucoma. Visual fields show doubtful field defects in the inferior quadrant which is confirmed from the OCT analysis showing definite thinning in the superior quadrant

The average RNFL thickness values in nasal and temporal sectors showed a decrease between mild and moderate glaucoma and it was not statistically significant. Thus, there is an inverse relationship between the severity of glaucoma and average and sectoral RNFL thickness, in which average RNFL thickness can be considered as the most important RNFL parameter.

4. Discussion

Glaucoma is one of the important causes of irreversible preventable blindness. It is important to accurately identify eyes with early structural damage and administer therapy before the development of functional loss. Studies with optical imaging systems have indicated that RNFL thickness may be valuable for the early diagnosis of glaucoma.

RNFL thinning is a sensitive indicator that shows the extent of glaucomatous damage and also RNFL loss precedes measurable ONH and VF damage by approximately six years. Accurate and objective methods of detecting disc and RNFL abnormalities and their progression would facilitate the diagnosis of POAG before VF defects would appear and help in monitoring the progression of glaucomatous optic neuropathy.

In this study, an attempt was made to analyse the correlation between visual field parameters by HFA and RNFL thickness and ONH parameters by OCT in different stages of glaucoma.

50% of the study subjects were aged > 60 years with a mean age of 60.12 years which was in correlation with that of 62.82 years in Chinmayeepabouli et al⁹ study and 60.54 years in Prempalkaur et al.¹⁰ study.

Male preponderance was noted in the present study with 60.91% of the patients belonging to the severe glaucoma group with Biarcuate scotoma being the most frequent visual field defect documented.

The mean deviation in the present study was -16.90 dB as opposed to -11.3 dB in a study by Alasil et al¹¹ which included 108 open-angle glaucoma subjects. Yalvac et al,¹² analysed 28 eyes in various stages of glaucoma and compared the results with those of 38 eyes of normal age-matched controls. The mean deviation noted in their study was -13.79 ± 9.47 dB. In another study by Liu et al¹³ which studied 100 open-angle glaucoma patients, MD was -12.2 dB. The mean deviation in our study was comparatively higher than all the other studies, most probably due to the higher number of patients with severe glaucoma included in this study. As the severity of glaucoma increased MD and PSD also increased.

But, the MD was -4.54 ± 0.25 dB in 13 patients of early glaucoma which was in accordance with -4.6 ± 0.3 dB in Mansoori et al¹⁴ study which included 83 patients with early glaucoma.

The mean average RNFL thickness in this study was 79.06 ± 13.51 μ m. The average RNFL thickness and mean RNFL thickness in all the sectors showed a gradual decline as the severity of glaucoma increased. The sectoral RNFL

thicknesses showed a gradual decline but the difference was statistically significant only in inferior and superior sectors between mild and moderate glaucoma. Thus, average RNFL thickness was the most important RNFL parameter followed by superior and inferior sector RNFL thickness in this study.

Yalvac et al,¹² showed an average RNFL thickness of $62.90 \pm 16.56 \mu\text{m}$ in the glaucoma group and $111 \pm 6.00 \mu\text{m}$ in the control group ($P < 0.05$). In the present study, 87 eyes of 50 glaucomatous patients showed an average RNFL thickness of $79.06 \pm 13.51 \mu\text{m}$.

Ahmed E. Abd El-Naby et al¹⁵ studied 60 glaucomatous eyes and compared RNFL thickness in various stages of glaucoma. On comparison of average RNFL thickness, mean superior, inferior, nasal and temporal sectoral thickness values between different grades of glaucoma, the present study showed a gradual decline from mild to severe glaucoma. The same observation was made by Ahmed E. Abd El-Naby et al.

As the severity of glaucoma increased average RNFL thickness showed a gradual decline which was statistically significant when compared between groups. Even though the average RNFL thickness values in nasal and temporal sectors showed a decline between mild and moderate glaucoma, they failed to show statistical significance. This can be explained by the fact that visual field defects associated with glaucoma usually occur initially in the superior and inferior visual fields. In our study, the parameters with the best discriminating power to differentiate mild from moderate glaucoma mostly belonged to superior and inferior regions and global RNFL. Similar findings have been reported by Nouri Mahdavi et al,¹⁶ and Leite et al.¹⁷

The strength of this study is that all the investigations were non-invasive, non-contact and reproducible. Changes in the RNFL thickness on OCT paralleled with the severity of glaucoma. So, in patients where fields cannot be recorded OCT findings will help in diagnosing glaucoma and in assessing the progression of the disease.

In cases of early glaucoma or borderline cases where there is a diagnostic dilemma, RNFL thickness analysis and ONH parameters on OCT gives an insight into the presence of glaucoma by correlating with the field defects.

The limitations of the study include a small sample size. As this is a cross-sectional study, there was no follow up for these cases and hence no longitudinal data was available. And, OCT could not be done in patients with hazy media.

In future, this study can be extended to compare RNFL thickness in normal controls and patients with early glaucoma before the occurrence of any visual field defect. The prospective study can provide us with longitudinal structural and functional data which can help in a detailed understanding of the progression of the disease.

5. Conclusion

To conclude structural changes on OCT correlated with functional damage shown on visual fields in POAG and OCT may prove to be a useful non-invasive imaging modality to monitor and follow up patients with early glaucoma before the evolution of functional loss (visual field defect).

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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