Vol: 07, Issue 03
OPHTHALMOLOGY PAKISTAN

Original Article

To determine the diagnostic accuracy of optical coherence tomography in the early detection of choroidal neovascularisation in patients with age related macular degeneration taking fluorescein angiography as gold standard.

Author's Affiliation

Mohammad Owais Sharif

Humera Zafar

Correspondence Author:

Correspondence to:
Dr. Mohammad Owais Sharif
COAVS / Institute of Ophthalmology,
Mayo Hospital Lahore.

Purpose: To determine the diagnostic accuracy of optical coherence tomography (OCT) with fundus fluorescein angiography (FA) in the early detection of choroidal neovessels (CNV) in patients with age related macular degeneration (AMD) taking FA as gold standard.

Materials and Methods: This cross-sectional study was conducted at Eye Unit III, Institute of Ophthalmology, King Edward Medical University / Mayo Hospital, Lahore. 205 patients were studied for early detection of CNV in patients with AMD by determining the diagnostic accuracy of OCT with FA.

Results: Out of 205 cases, 45.37% (n=93) were between 50-65 years of age and 54.63% (n=112) were between 66-80 years of age, mean ± SD was calculated as 65.52 ± 6.93, 57.56% (n=118) were male and 42.44% (n=87) were females. Frequency of CNV on FA was recorded in 38.54% (n=79). Diagnostic accuracy of OCT vs FA in the early detection of CNV in patients with AMD was calculated which shows sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate as 89%, 73.02%, 67.62%, 92% and 79.51% respectively.

Conclusion: This concluded a higher diagnostic accuracy of OCT vs FA in the early detection of CNV in patients with AMD.

Keywords: Age Related Macular Degeneration, Choroidal Neovascularization, Optical Coherence Tomography.

Introduction

One of the leading causes of blindness in people over 65 years of age is age related macular degeneration (AMD). AMD is a degenerative disease characterized by specific clinical findings like the presence of drusen, retinal pigment epithelial (RPE) changes and/or choroidal neovascularization (CNV). The prevalence of AMD in people over 40 years of age is 6.5% in USA.[1] Overall prevalence of neovascular AMD is 1.2% in people aged 50 years.[2] The risk of deterioration of vision is considerably higher when drusen are large and numerous and are associated with disturbance in pigment cell layer underlying macula. Recent research suggests that higher cholesterol levels are associated with increased drusen.[3]

CNV is a characteristic of wet AMD. Classification of CNV into type-1 and type-2 is based on the location of the neovascular complex with respect to RPE layer. Lesions are classified as type-1 when confined under RPE and type 2 when vessels proliferate in sub-retinal space. Fundus fluorescence angiography (FA) is the gold standard test for the diagnosis of CNV and depending upon the FA findings CNV are classified as CLASSIC and OCCULT types. The frequency of CNV in AMD was 43.48% on FA in a study conducted in China.[4] Statistically the sensitivity of OCT is 97% and specificity is 37% in CNV detection, taking FA as gold standard (its specificity and sensitivity is 100 %).[5] In another study conducted by Do et al, the sensitivity of OCT is 40% while taking FA as gold standard.[6] In recent past the main criteria to treat and re-treat the neo-vascular AMD lesions by photo dynamic therapy or anti VEGF therapy was the presence or absence of florescence leakage and the angiographic appearance of the lesion. With the emergence of OCT, its accuracy and findings became important for determination of activity of CNV lesions.[7,8] OCT is non-invasive and cost effective test, that reduces the number of visits, has better patient compliance and gives more details of Retinal Layers, whereas FA has certain drawbacks including patient preparation, being invasive, chances of drug reaction, multiple visits, hepatic and renal toxicity and difficulty to perform in the presence of media opacity.[5] Recent advances in OCT have improved its diagnostic capabilities. High resolution and three-dimensional view of images have improved its efficiency and as per its advantages over FA it may prove to be a better and safer diagnostic modality for the detection of CNV in patients of AMD and hence save the patients from the adverse effects of fluorescein. The current study was planned to determine the diagnostic accuracy of OCT vs FA in detection of CNV as there is no previously local study done on this age group and many available international studies show a lot of controversy in their results.

Materials and Methods

This study was conducted at eye unit III, Institute of Ophthalmology, King Edward Medical University / Mayo Hospital, Lahore from 13-5-2014 till 12-11-2014. It was a cross sectional study. Non probability purposive sampling was done. 205 cases were taken with a confidence level of 95%, 3% margin of error for sensitivity i.e. 97% and 10% margin of error for specificity i.e. 37% of OCT in the detection of CNV in patients of AMD by using 43.48% as expected prevalence of AMD. Patients of both genders between 50 to 80 years with AMD and suspected CNV on indirect ophthalmoscopy and patients diagnosed as having AMD in the last 6 months were included in the study. Patients having significant media opacity (in cornea, aqueous, lens, vitreous) on slit lamp examination, known allergy to fluorescein dye or any other kind of allergy, any evidence of macular diseases like pattern dystrophy, diabetic macular edema, vitreomacular traction etc., other than AMD, any previous history of surgical or laser treatment to the eye and diabetic retinopathy on indirect ophthalmoscopy were excluded from the study.

Data Collection Procedure

After approval from institutional review board of hospital for ethical issues, 205 patients fulfilling the inclusion and exclusion criteria were selected from outdoor of eye unit III, Institute of Ophthalmology King Edward Medical University, Mayo Hospital, Lahore. After taking informed written consent, both tests were performed on each patient. The risks like (generalized skin itching, sensitivity on exposure to light due fluorescence dye, nausea, vomiting) and benefits (early detection and proper management in stopping or slowing down the disease) were explained to the patients. The initial preparation for both the tests was same i.e. pupil could be dilated. For both the tests, the patients were made to sit comfortably in front of the camera and shown a target to fix the eyes. For OCT the machine was adjusted manually as well as by auto-focusing on the Fundus and getting green signal from machine, that focus was sharp enough, the image was taken. Both the tests were performed by the investigator himself, reporting was done by a single consultant to avoid bias and all the data were collected through pre designed proforma.

Data Analysis

The data were analyzed on SPSS version 17. The frequency and percentages were calculated for qualitative variables like CNV on OCT and FA, and Gender. Mean and standard deviation was calculated for quantitative variable like age. 2x2 tables was used for calculation of sensitivity and specificity, positive predictive value, negative predictive value and accuracy of OCT for detection of CNV in AMD patient

taking FA as gold standard.

Results

205 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the diagnostic accuracy of OCT with FA in the early detection of CNV in patients with AMD taking FA as gold standard. Age distribution shows that 45.37% (n=93) were between 50-65 years of age and 54.63% (n=112) were between 66-80 years of age, mean ± SD was calculated as 65.52 ± 6.93 years. Patients were distributed according to gender, where 57.56% (n=118) were male and 42.44% (n=87) were females. Frequency of CNV on FA was recorded in 38.54% (n=79) while 61.46% (n=126) had no findings of CNV (Table no. 1). Diagnostic accuracy of OCT with FA in the early detection of CNV in patients with AMD taking FA as gold standard was calculated. Out of 79 cases of CNV, 34.63% (n=71) were true positive, 16.59% (n=34) were false positive, 3.90% (n=8) were false negative and 44.88% (n=92) were true negative. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate was calculated as 89%, 73.02%, 67.62%, 92% and 79.51% respectively, (Table no. 2).

Table No. 1
FREQUENCY OF CNV ON FA (n=205)

CNV	No. of patients	%
Yes	79	38.54
No	126	61.46
Total	**205**	**100**

Table No. 2
DIAGNOSTIC ACCURACY OF OCT IN EARLY DETECTION OF CNV IN PATIENTS WITH AMD (n=79).

OCT	FA	
	CNV (Positive)	CNV (Negative)
Positive	True positive (a) 71 (34.63%)	False positive (b) 34 (16.59%)
Negative	False negative (c) 8 (3.90%)	True negative (d) 92 (44.88%)

Sensitivity = a / (a + c) x 100 = 90%
Specificity = d / (d + b) x 100 = 73%
Positive predictive value = a / (a + b) x 100 = 67.62%
Negative predictive value = d / (d + c) x 100 =92%
Accuracy rate = a + d / (a + d + b + c) x 100 = 79.51%

Discussion

Fundus fluorescein angiography (FA) interpreted by an ophthalmologist in the recent past was the reference standard for the detection of active neovascular AMD among those eyes already treated because it directly detects the presence of the active neovascularization. However, FA is an invasive and a time consuming test with potentially serious, although rare, side effects. Other alternative monitoring technologies are available, of which the most widely used is optical coherence tomography (OCT).[9]

The gold standard of ocular imaging in exudative age-related macular degeneration (AMD) has traditionally been FA. Previous clinical studies assessing treatments for AMD have generally based their treatment on the appearance of the CNV on FA. With the advent of anti-VEGF therapy, dependence on FA has decreased and physicians are starting to look at other imaging modalities, in particular optical coherence tomography (OCT), to help guide management decisions. In the past with laser photocoagulation and photodynamic therapy with verteporfin, the Macular Photocoagulation Study (MPS) and Treatment of AMD and Photodynamic Therapy (TAP) Trials gave very strict guidelines when to retreat the patients based on the CNV appearance on FA.[10,11]

Numerous modalities are available to try to detect CNV. Amsler grid testing, preferential hyperacuity perimetry (PHP), OCT, and FA are tools that may be used to detect CNV. This study was planned to determine the diagnostic accuracy of OCT vs FA in detection of CNV. As there is no previously local study done on this age group and many international studies available, which show a lot of controversy in their results. So, it was inevitable to determine its diagnostic accuracy in this local population to save the patients from the adverse effects of fluorescein dye.

Optical coherence tomography (OCT), a non-invasive and noncontact method of imaging the posterior structures of the eye, has become a frequently used imaging technique to detect and monitor morphologic changes (e.g., subretinal fluid, intra-retinal fluid, elevation of the RPE) associated with CNV. Although OCT is commonly used to image eyes with AMD, it also is unknown whether periodic OCT testing would improve this ability to identify new-onset CNV relative to standard care practices, or provide information that supplements PHP testing, or is of no value in monitoring AMD patients at risk of CNV.[6,12,13]

In this study, out of 205 cases, frequency of CNV on FA was recorded in 38.54% (n=79). Diagnostic accuracy of OCT with FA in the early detection of CNV in patients with AMD taking FA as gold standard was calculated. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate were 89%, 73.02%, 67.62%, 92% and 79.51% respectively. The findings of this study regarding diagnostic accuracy of OCT are in agreement with a study[5] showing the sensitivity of OCT in 97% while specificity was 37% in CNV detection which is lower than this study. According to Do et al, the sensitivity of OCT is 40% while taking FA as gold standard[6], which is significantly lower than in this study. Khurana et al, reported a sensitivity of 90% and specificity of 47% for SDOCT to detect CNV on FA.[14]

Do et al. reported a sensitivity of only 40% for the detection of new-onset CNV on time-domain OCT. The low sensitivity may be explained by the use of time-domain OCT. The pathological features may be overlooked more easily due to the less dense scan pattern, lower image resolution, and high movement artifacts.[6,13] Nils F Mokwa compared color fundus photographs (FP), FA and spectral domain optical coherence tomographs (SDOCT) for the detection of AMD, CNV, and CNV activity.[17] He diagnosed AMD on FA in 75 eyes. SDOCT and FA showed sensitivity (specificity) of 89% (76%) and 92% (82%), respectively. CNV was present on FA in 68 eyes. Sensitivity (specificity) was 78% (100%) for FA and 94% (98%) for SDOCT. CNV activity was detected by SDOCT or FA in 60 eyes with an agreement in 46 eyes. Sensitivity was 88% for SDOCT and 88% for FA. FA showed sensitivity of 38% and specificity of 98%. He concluded that CNV lesions and activity may be missed by FA alone, but FA may help identifying drusen and pigmentary changes. SDOCT is highly sensitive for the detection of AMD, CNV, and CNV activity. However, it cannot fully replace FA.[15] Disagreement between both imaging modalities may be explained by the fact that FA and OCT imaging provides different information about retinal pathology. FA is used to obtain information about the perfusion and the growth of new vessels as well as the integrity of the blood retinal barrier. Fluorescein leakage over time can be seen during angiography.[16]

This information is missing on OCT images. OCT provides detailed information about pathological changes like, the presence of cystoids spaces. However, it is not possible to detect whether they are caused by fluid accumulation from acute leakage from pathological vessels. In contrast, CNV activity seen on FA may be missed on OCT if only intra retinal cystoids spaces and sub retinal fluid accumulation are considered to represent CNV activity on SDOCT.[16,17] Our findings are primary in this local population, which needs some other studies to be conducted to confirm the findings of this study. However, OCT being a modern non-invasive imaging technique with a high depth resolution, based on low coherence interferometry (LCI), that is able to reconstruct (tomographic) sectional images of the object under study. The first application of LCI in ophthalmology was to measure the eyeball length. OCT is similar to ultrasound imaging, but as an optical echo technique has much higher resolution. The key benefits of OCT are: live sub-surface images at near-microscopic resolution; instant, direct imaging of tissue morphology; no preparation of the sample or subject; no ionizing radiation. OCT is useful in situations where biopsy cannot be performed, where sampling areas with conventional biopsies are likely, and that involve guiding surgical/microsurgical procedures.

Conclusion

This study concluded a higher diagnostic accuracy of OCT with FA in the early detection of CNV in patients with AMD.

References

1. Klein R, Chou CF, Klein BE, Zhang X, Meuer SM. Prevalence of age-related macular degeneration in the US population. Arch Ophthalmol. 2011;129:75-80.
2. Owen CG, Jarrar Z, Wormald R, Cook DG, Fletcher AE, Rudnicka AR. The estimated prevalence and incidence of late stage AMD in the UK. Br J Ophthalmol. 2012;96(5):752-6.
3. Sene A, Khan AA, Cox D, Nakamura RE, Santeford A, Kim BM, et al. Impaired cholesterol efflux in senescent macrophages promotes age-related macular degeneration. Cell Metabolism. 2013;17(4):549-61.
4. Shi XH, Wei WB, Tian B, Yang LH, Ding N, Wang ZH, et al. Analysis of clinical features of choroidal neovascularization. [Zhonghua yan ke za zhi] Chinese Journal of Ophthalmology. 2008;44(9):780-5.
5. Henschel A, Spital G, Lommatzsch A, Pauleikhoff D. Optical coherence tomography in neovascular AMD compared to fluorescein angiography and visual acuity. 2009;19:831-5.
6. Do DV, Gower EW, Cassard SD, Boyer D, Bressler NM. Detection of new-onset choroidal neovascularization using optical coherence tomography: The AMD DOC Study. Ophthalmology. 2012;119:771-8.
7. Jalil A, Mercieca K, Chaudhry NL, Stanga PE. Choroidal nonperfusion with significant subretinal exudation after PDT of predominantly classic CNV: an OCT and FA study. Eur J Ophthalmol. 2009;19:490-3.
8. Regatieri CV, Branchini L, Duker JS. The role of spectral-domain OCT in the diagnosis and management of neovascular age-related macular degeneration. Ophthalmic Surgery, Lasers and Imaging Retina. 2011;42(4):S56-66.
9. Sayanagi K, Sharma S, Yamamoto T, Kaiser PK. Comparison of spectral-domain versus time-domain optical coherence tomography in management of age-related macular degeneration with ranibizumab. Ophthalmology. 2009;116:947–55.
10. Khurana RN, Dupas B, Bressler NM. Agreement of time-domain and spectral-domain optical coherence tomography with fluorescein leakage from choroidal neovascularization. Ophthalmology. 2010;117:1376–80.
11. Keane PA, Patel PJ, Ouyang Y. Effects of retinal morphology on contrast sensitivity and reading ability in neovascular age-related macular degeneration. Invest Ophthalmol Vis Sci. 2010;51:5431-37.
12. Sayanagi K, Sharma S, Yamamoto T, Kaiser PK. Comparison of spectral-domain versus time-domain optical coherence tomography in management of age-

related macular degeneration with ranibizumab. Ophthalmology. 2009;116:947–55.
13. Khurana RN, Dupas B, Bressler NM. Agreement of time-domain and spectral-domain optical coherence tomography with fluorescein leakage from choroidal neovascularization. Ophthalmology. 2010;117:1376–80.
14. Yannuzzi LA. Indocyanine green angiography: a perspective on use in the clinical setting. Am J Ophthalmol 2011;151:745.ate stage AMD in the UK. Br J Ophthalmol. 2012;96(5):752-6.
15. Truong SN, Alam S, Zawadzki RJ. High resolution Fourier-domain optical coherence tomography of retinal angiomatous proliferation. Retina. 2007;27:915–25.
16. Regillo CD, Brown DM, Abraham P. Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER Study year 1. Am J Ophthalmol.2008;145:239–48.
17. Mokwa NF, Ristau T, Keane PA, Kirchhof B, Sadda SR, Liakopoulos S. Grading of age-related macular degeneration: comparison between color fundus photography, fluorescein angiography, and spectral domain optical coherence tomography. J Ophthalmol. 2013;2013.