Original Article

Low Rates of Optical Coherence Tomography Utilization in the Diagnosis and Management of Retinovascular Diseases in a Lower Middle-Income Economy

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ABSTRAC

Background: Optical coherence tomography (OCT) is widely used as the standard of care in evaluating macular and retinovascular diseases. However, the degree of OCT utilization is yet to be researched in a resource-limited country where wide gaps exist in access to healthcare. Aim: To determine the rate of utilization of the OCT in diagnosis, pre-treatment, and post-treatment evaluation of macular and retinovascular diseases treated with intravitreal anti-vascular endothelial growth factor injection (IVI). Patients and Methods: Retrospective, consecutive, and non-comparative case series of eyes diagnosed and treated from Jan 2017 to Jan 2022 for seven macular and retinovascular diseases in five eye clinics in Nigeria. Data extracted include demographics, indication for IVI, eye treated, use or non-use of OCT at the diagnosis (pre-treatment) and after the last IVI (post-treatment), and central macular thickness (CMT) of pre-treatment OCT scans. Results: Seven hundred and forty two eyes were diagnosed with retinovascular and macular diseases (389 right eyes and 353 left eyes). The male to female ratio was 430: 312 eyes. The mean age was, 63.89 years (SD 12.58). Four hundred and fifty two eyes (60.9%) had a pre-treatment OCT, 235 eyes (31.7%) had a post-treatment OCT, and 190 eyes (25.6%) had both pre- and post-treatment OCTs. The rate of pre-treatment OCT varied with the diagnosis (P = 0.000); DME had the highest rate, 74.4%, and HRVO had the lowest, 40%. Post-treatment OCT rate varied with the diagnosis (P = 0.009); non-AMD CNVM had the highest rate, 49.1%, and PCV had the lowest, 24.6%. Pre-treatment OCT rate was influenced by clinic location (P = 0.000); higher in clinics having an OCT. Post-treatment OCT was not influenced by clinic location (P = 0.37). A CRVO eye had the highest maximum CMT (1031 microns) of all the pre treatment eyes and the lowest minimum CMT of all the pre treatment eyes was in a BRVO eye (138 microns). Mean CMT was highest in HRVO (475.33 microns) and lowest in CNVM (307.62 microns). Conclusion: Though OCT is the standard of care for managing retinovascular and macular diseases, this research quantifies the extent of its use in Nigeria and finds it to be low. A post-treatment OCT rate of 32% suggests that urgent steps are required to improve access to OCT for IVI patients.

KEYWORDS: Central macular thickness, intravitreal anti-vascular endothelial growth factor, lower middle-income country, macular disease, optical coherence tomogram, retinovascular diseases

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Introduction

Optical coherence tomography (OCT) was developed by Huang and Fujimoto and became commercially available in 1996.[1] Though initial clinical adoption of

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this imaging technology was slow, by 2004, millions of OCT imaging procedures had been performed.[1,2] Since then, the OCT has been used in evaluating different parts of the eye, including the anterior segment, [3,4] retina, [5] choroid,^[6] and optic nerve,^[7,8] in health and various disease states. The initial time domain OCT which gave low-resolution images of the retina has given way to faster scans that give more detailed and higher resolution images using the spectral domain and fourier domain features of modern-day OCT machines. [9-12] Enhanced depth imaging is another later feature of OCT.[6,13] The OCT is now commonly used alongside clinical evaluation of the retina for several retinal diseases. Because of the advantages offered by modern OCT, including high resolution, reproducibility, non-invasive, and easy-to-acquire images, it has become popular among several retinal specialists for the screening, diagnosis, and evaluating the response to treatment of retinovascular diseases such as diabetic macular edema (DME), and retinal vein occlusion (RVO), and macular diseases such as age-related macular degeneration (AMD). For these retinovascular diseases, the use of the OCT has become quite common, so much so that it is now regarded as the standard of care and used for evaluating the outcome of treatment and other interventions in pivotal clinical trials evaluating the effect of new therapy on retinal diseases.[14-17]

Despite its usefulness and everyday use in several parts of the developed world, the extent of use of the OCT in evaluating retinovascular diseases in a lower middle-income country (LMIC), where out-of-pocket payment is common, is yet to be assessed. In such LMIC, it is likely that the OCT may not be equally accessible to all patients in need of it, and therefore, limits to its use exist. This study seeks to determine the degree of OCT utilization at initial presentation (time of diagnosis) and to monitor response to treatment and outcome of intravitreal anti-vascular endothelial growth factor (VEGF) injections (IVI) for the treatment of retinovascular and macular diseases in LMIC.[18] It also provides insight into the pre-treatment measurements of the central subfoveal macular thickness (CMT) in common retinovascular and macular diseases.

METHODOLOGY

A retrospective non-comparative consecutive cases series was done, using information from clinical records and OCT images of consecutive patients diagnosed with AMD, DME, BRVO, CRVO, HRVO, non-AMD choroidal neovascular membrane (CNVM), and polypoidal choroidal vasculopathy (PCV), who consented to treatment using IVIs. Ethical approval for

the study was sort from the Eye Foundation Hospital Health Research Ethics Committee. A waiver was provided for this research since it involved the review of case records. This research adhered to the principles of the Helsinki declaration. The patients were seen in five ophthalmic clinics in Nigeria from January 2017 to January 2022. Using the IVI log, the case records of all patients who had IVI for the above diagnoses were assessed to determine the use or non-use of the OCT 1.) at the time of diagnosis and 2.) to evaluate the treatment response during IVI therapy. The OCT scan at the initial diagnosis was considered the pre-treatment scan. Subsequent OCT scans after initiating anti-VEGF treatment, specifically the OCT scan after the last IVI, were considered the post-treatment scan. We took note of eyes that had both pre- and post-treatment OCT scans. We took note of the CMT (defined as average thickness within the 1mm grid) from the pre-treatment OCT scans. All information from the case records was anonymized.

The five clinic locations include three in urban locations, one in semi-urban, and one in rural locations. Data were entered into an excel spreadsheet and analyzed using IBM SPSS version 22.0 (IBM Corp. Armonk, NY, USA). We summarized categorical variables as frequencies, means, and percentages. The CMT was represented as means and standard deviation. Kruskal Wallis was used to analyze non-parametric data relating to the frequency of OCT scans for retinovascular diseases, while cross-tabulation using Pearson Chi-Square was used to analyze the frequency of OCT scans among the clinic locations.

RESULTS

During the study period, 742 eyes were diagnosed to have the seven retinovascular and macular diseases considered. The mean age was 63.89 years (SD 12.58), range 10–94 years. There were 389 right eyes and 353 left eyes: males and females, 430 and 312 eyes, respectively. Of the 742 study eyes, 452 (60.9%) had an OCT examination at the time of diagnosis (pre-treatment). Two hundred and thirty five eyes, (31.7%), had an OCT for evaluating treatment outcome after the last IVI treatment (post-treatment), and fewer eyes, 190 (25.6%), had OCT examination at both the time of initial diagnosis and after the last IVI, (pre- and post-treatment). The proportion of eyes that had OCT imaging can be seen in Table 1.

In all seven indications for IVI, the highest proportion of eyes had a pre-treatment OCT evaluation, as shown in Table 1, and this varied based on the indication for IVI (P = 0.000). Subsequently, in several of the diagnoses, approximately half the number that had the pre-treatment

OCT had post-treatment OCT performed for the evaluation and monitoring of treatment outcome, which was also influenced by the indication for IVI (P=0.009). The numbers that had both pre- and post-treatment OCT were consistently lower than those that had the post-treatment OCT and only marginally fell short of statistical significance for a relationship with the indication (P=0.051). As depicted in Table 1, DME had the highest compliance to pre-treatment OCT (74.4%), while the lowest was 40% in HRVO. Post-treatment OCT compliance was highest in non-AMD CNVM at 49.1% and lowest in PCV at 24.6%. The highest compliance rate to pre- and post-treatment OCT was in non-AMD CNVM at 40%, and the lowest compliance was in HRVO at 13.3%.

Compliance in the five clinics is depicted in Table 2. Compliance with pre-treatment OCT was highest in

Table 1: Clinical diagnosis and proportion of eyes that had OCT imaging

had OCT imaging								
Diagnosis/	Pre-treatment	Post-treatment	Pre and Post OCT					
Indication (No of	OCT	OCT						
Eyes)								
AMD (121) n	69	30	25					
%	57	24.8	20.7					
CNVM	34	27	22					
(non-AMD) (55) n								
%	61.8	49.1	40					
BRVO (163) n	100	53	42					
%	61.3	32.5	25.8					
CRVO (141) n	94	40	37					
%	66.7	28.4	26.2					
HRVO (15) n	6	5	2					
%	40	33.3	13.3					
DME (133) n	99	52	40					
%	74.4	39.1	30.1					
PCV (114) n	50	28	22					
%	43.9	24.6	19.3					
P	0.000	0.009	0.051					

clinics 1 and 2 (urban clinics), followed by clinic 5 (rural). These three clinics had an OCT equipment installed within the hospital. Clinics 3 and 4 did not have OCT equipment and had to send patients to neighboring clinics for an OCT examination. Pre-treatment OCT showed a statistically significant difference among the clinics (P = 0.000). In contrast, the clinic effect on post-treatment OCT and the combined pre- and post-treatment OCT was not statistically significant (P = 0.37 and 0.33, respectively) Table 2.

The highest pre-treatment mean CMT was in HRVO, 407.41 microns. A CRVO eye had the highest maximum CMT of 1031 microns of all the pre-treatment eyes. The lowest mean CMT was in non-AMD CNVM, 307.62 microns, Table 3. However, the lowest minimum CMT of all the pre-treatment eyes was 138 microns in a BRVO eye. All seven diagnoses had a mean CMT above

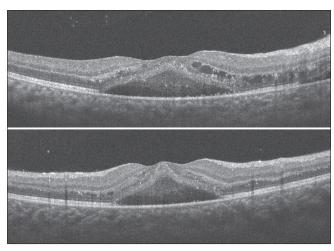


Figure 1: Horizontal and vertical (superior and inferior) cross sectional OCT scans of an eye revealing subretinal and intraretinal fluid. There are also intraretinal hyper reflective dots indicative of exudation into the retina. The superior frame also shows hyper reflective dots lining on the RPE in the area of neurosensory retinal detachment. These hyper reflective dots may be indicative of degenerative photoreceptor cell

Table 2: Compliance to pre- and post-treatment OCT in the five clinics						
Clinic Location	Pre-Treatment OCT	Post-Treatment OCT	Pre and Post Treatment OCT			
Clinic 1 Urban n	309	160	134			
%	60.7%	31.4%	26.3%			
Clinic 2 Urban n	130	66	50			
0/0	69.5%	35.3%	26.7%			
Clinic 3 Urban n	2	3	1			
%	13.3%	20.0%	6.7%			
Clinic 4 Semi Urban n	2	2	2			
%	18.2%	18.2%	18.2%			
Clinic 5 Rural n	9	4	3			
%	45.0%	20.0%	15.0%			
Total <i>n</i>	452	235	190			
%	60.9	31.7%	25.6%			
P	0.000	0.37	0.33			

Table 3: Pre-treatment central macular thickness (CMT) at presentation for seven retinovascular and macular diseases

	AMD	CNVM	BRVO	CRVO	HRVO	DME	PCV
Mean CMT	375.17	307.62	412.57	459.49	475.33	407.41	326.88
Std. Deviation	172.753	97.449	149.503	224.972	249.223	158.236	125.933
Min. CMT	168	181	138	144	246	200	146
Max. CMT	830	529	762	1031	816	838	627

CMT: Central macular thickness, CNVM: Choroidal neovascular membrane, BRVO: Branch retinal vein occlusion, CRVO: Central retinal vein occlusion, HRVO: Hemiretina vein occlusion, DME: Diabetic macular edema, PCV: Polypoidal choroidal vasculopathy

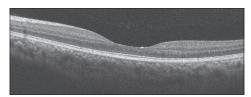


Figure 2: Normal appearing cross sectional OCT scan of the macula showing the outer retina (including the external limiting membrane, ellipsoid zone, and retinal pigment epithelium) and a healthy inner retina

300 microns. Similarly, all the diagnoses had a minimum CMT below 250 microns and a maximum above 500 microns. The maximum CMT was above 800 microns in four out of seven diagnoses, Table 3.

DISCUSSION

This research investigated the rate of utilization of OCT imaging for the pre- and post-treatment evaluation of retinovascular and macular diseases in a LMIC and finds it to be low. The OCT is an essential, must-have facility for evaluating and monitoring the treatment of several retinovascular diseases. Retinovascular diseases rank among the leading cause of retinal blindness according to several reports from Africa and around the globe.^[19-22]

Prior to the availability of the OCT, retinovascular diseases were mainly diagnosed and evaluated using clinical examination, including fundoscopy, fundus imaging using a camera, and fluorescein and indocyanine green angiography to study the retinal and choroidal vascular circulation. The OCT provides a valuable objective, reproducible, and quantitative method of assessing retina thickness, which is a surrogate for retina edema. Because of the high axial resolution of the OCT, high-definition images of the retina can be obtained, which reveal intraretinal cystic spaces and intraretinal deposits of exudative material such as lipids and cells [Figure 1]. The OCT also provides useful biomarkers which help in prognosticating vision and treatment outcomes. These biomarkers include outer retinal layers such as the Ellipsoid Zone (EZ) and External Limiting Membrane (ELM) [Figure 2].

There are several reports on using OCT to diagnose and treat retinal diseases among Africans. [23-26] Our

study is the first study evaluating the frequency of OCT use in real life, among Africans, for the diagnosis of retinovascular diseases and monitoring of IVI treatment. We discovered that over half of the eyes studied had an OCT examination at diagnosis, and about a third of eyes had OCT for evaluating treatment outcomes following IV anti-VEGF treatment. A quarter of eyes had both pre- and post-treatment OCT evaluation. Considering the usefulness of the OCT and its role in several guidelines for treating retinovascular diseases, the rate of OCT utilization we recorded is below the desired. Ideally, every eye should have an OCT pre- and post-treatment. Limitations to using the OCT are primarily in situations of unclear media or inability of the eye to fixate.

Studies on the barriers to accessing healthcare in Nigeria have identified three barriers: cultural, resource-related, and physical.^[27] We suggest that more specific reasons for the non-use of the OCT among the study patients and other patients in the region include economic factors such as lack of funds (consequence of high out of pocket payment for healthcare),[28,29] OCT equipment not being available in the clinic, breakdown of the OCT equipment, and lack of knowledge on the part of the patient and possibly the treating physician on the value of the OCT in disease management. Some of these gaps can be closed by providing low-cost, affordable OCT equipment which produces good quality, reproducible images for LMIC,[30] and by educating the patient and treating physician on the importance of the OCT in disease management. Advocacy for providing such low-cost equipment should be targeted at biomedical companies that manufacture OCT equipment. In some situations, a private-public partnership model has been adopted to provide essential medical equipment.[31] This model has been found to be successful in several instances, with the patient being the ultimate beneficiary of such a collaboration or partnership.^[32]

In our study, we showed that having an OCT machine in the clinic improved compliance and uptake of the OCT examination. The three clinics with OCT equipment had a significantly higher proportion of scans performed than those without OCT equipment. This finding was replicated even in the rural clinic 5, which had higher compliance to pre-treatment OCT compared to urban clinic 3 and semi-urban clinic 4. We would expect that because of the higher socioeconomic status of patients attending clinics 3 and 4, compliance would be more than in clinic 5, but this was different in real life, as shown by our study. Therefore, this makes a case for providing an OCT machine in clinics where retinovascular and macular diseases are diagnosed and managed since referring patients to neighboring clinics may reduce compliance. However, only the pre-treatment OCT appeared to benefit from the clinic effect, as the rate of post-treatment OCT was not significantly different between the clinics. This suggests that patients are reluctant to have another OCT done after the initial pretreatment OCT scans. More should be done to improve the patient's understanding of the need for monitoring IVI treatment using post-treatment OCT.

Because the OCT can accurately measure the CMT, we could establish the mean CMT of various retinal diseases.[33] This research further demonstrates the real-life severity of macular edema at presentation for several retina diseases. Our findings show that the central macular thickness in macular, choroidal, and outer retinal diseases such as AMD, CNVM, and PCV was less than that in those retinal diseases involving the inner retinal vasculature such as the RVOs (BRVO, CRVO, and HRVO) and DME. Further, prospective studies including a large sample size will provide more information on the severity of macular edema in the various diseases and response to treatment using IVI. These retinovascular and macular diseases typically show a favorable response to intravitreal anti-VEGF injections as shown by reports from other researchers.[34,35] The OCT is, therefore, invaluable in understanding disease severity and comparing disease effect on retina anatomy following treatment.

Study limitations include being retrospective; it did not directly inquire from the patients about the reason for the non-uptake of the OCT examination. In some cases, the treating ophthalmologist may have decided to use only findings on clinical examination and not requested an OCT. Notwithstanding, the information provided by this research will be useful in planning retina clinics and interventions using the OCT and IVI treatment for retinovascular and macular diseases. Our findings will be helpful when making socioeconomic decisions in managing retinovascular and macular diseases requiring OCT evaluation in LMIC. We provide information on the magnitude of effort required to improve compliance to OCT use for diagnosing and managing retina diseases. The OCT will only become more significant in caring for retina-related and other ophthalmic diseases. The OCT is already being used for self-monitoring some macular and retinovascular diseases as a home device. Therefore, like in more developed countries, access to OCT equipment is essential and should be provided for all patients who need it. This research also provides the CMT measurement for common macular and retinovascular diseases in Africans.

To conclude, because of the increasing usage of the OCT in managing retinovascular and macular diseases (including DME and AMD), which are leading causes of blindness, it is necessary that health authorities and all stakeholders should work to improve OCT access for all who need to have this examination. Several treatment guidelines for retinovascular diseases, including landmark clinical trials, now use the OCT. Therefore, disease management for LMIC patients must also be tailored according to the guidelines for which OCT examination is required. This provision of OCT for all falls within the scope of the United Nations' "Vision for Everyone" initiative.[37] The provision of low-cost, high-quality, and affordable OCT equipment should be a priority for LMICs, given the usefulness of the equipment for managing several ophthalmic diseases, specifically retinovascular and macular diseases. Achieving this goal will significantly improve the care of such retinal diseases diagnosed and managed using the OCT.

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Conflicts of interest

There are no conflicts of interest.

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