Indication for Anti-VEGF Treatment for Neovascular Age-Related Macular Degeneration Based on Optical Coherence Tomography Interpretation: Decision Agreement Rate between Orthoptist and Ophthalmologist

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ABSTRACT

Objective: Although orthoptists play an integral role in the care of patients with chronic eye diseases, the clinical decision making of orthoptists within this setting has not often been investigated. The aim of this study was to evaluate the inter-rater agreement between orthoptists and an ophthalmologist in determining whether anti-VEGF treatment for neovascular (wet) age-related macular degeneration (AMD) is required based on optical coherence tomography (OCT) interpretation.

Methods: A retrospective audit was conducted of patient data from a private ophthalmology practice. Data collected included details pertaining to patient demographics and clinical assessment, OCT retinal thickness, and the treatment decisions of five orthoptists and one senior vitreoretinal ophthalmologist when interpreting OCT scans. The inter-rater agreement between the orthoptists and the ophthalmologist was calculated as a percentage and the kappa (κ) statistic computed.

Results: Of a total 669 treatment decisions made, on 619 occasions (92.5%) agreement was found between the orthoptists and the ophthalmologist ($\kappa = 0.85$; 95%CI 3.43 - 1.26, $p < 0.001$) representing an almost perfect agreement.

Conclusion: Agreement between the orthoptists and ophthalmologist in AMD clinical decision making is very high suggesting that orthoptists could potentially have a greater involvement in shared-care models within specialist eye clinics.

Keywords: neovascular age-related macular degeneration, orthoptist, inter-rater agreement, anti-VEGF clinical decision making, optical coherence tomography

INTRODUCTION

As a consequence of population ageing, it is well known that the demand for eye care services is rapidly increasing. The most prevalent causes of vision impairment in developed countries are those related to ageing: age-related macular degeneration, cataract, glaucoma, diabetic retinopathy and refractive error.[1] Age-related macular degeneration (AMD) is the most common cause of irreversible vision loss world-wide and in Australia accounts for 50% of all cases of legal blindness in those aged 40 or older.[2]

AMD is a progressive eye condition that results in loss of central vision. Treatment options in the most severe form of the disease, neovascular AMD (nAMD), aim to slow disease progression. The current treatment method of choice involves intravitreal injection of an anti-vascular endothelial growth factor (VEGF) drug. Injections are continued indefinitely and usually administered on a needs-only basis dependent on disease activity.[2,3] To monitor disease progression, patients with nAMD undergo regular ophthalmic examinations involving an assessment of the fundus, including retinal imaging with optical coherence tomography (OCT). Whilst fundus fluorescein angiography (FFA) is considered the gold-standard for the differential diagnosis of nAMD, OCT imaging is increasingly used as a diagnostic tool prior to angiography[4] and performed to determine clinical management. Information obtained from the OCT scan, such as the presence/absence of fluid and change in retinal thickness, greatly influences the re-treatment decision.[5,6] A normal appearance on OCT is shown in Figure 1 and presence of fluid with increased retinal thickness is shown in Figure 2.

Whilst ophthalmologists are responsible for the management of patients with nAMD, orthoptists are increasingly involved in supporting patient care through their involvement in the visual assessment and OCT imaging of patients with nAMD. Whilst orthoptists

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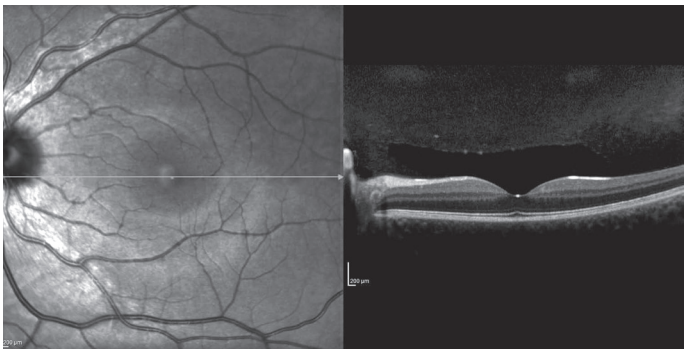

Figure 1. Macular OCT scan showing normal foveal contour and retinal thickness and no areas of hyporeflectivity.

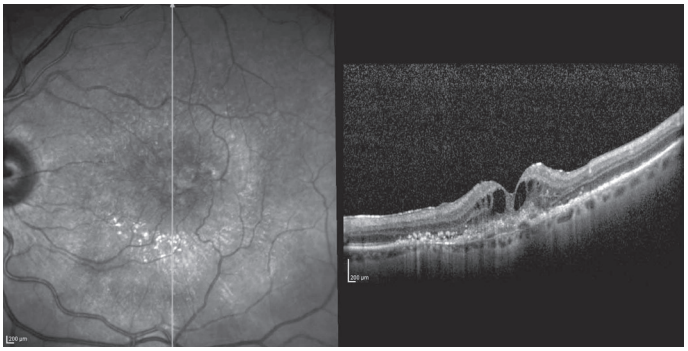

Figure 2. Macular OCT scan showing areas of hyporeflectivity indicating presence of fluid, with increased retinal thickening and loss of foveal contour.

commonly undertake OCT imaging, interpretation is not a conventional role undertaken during clinical assessment. Traditionally, the expertise of orthoptists has been in strabismus, ocular motility and binocular function investigation and management. In Australia, this role has evolved significantly to include general ophthalmic care within the secondary and tertiary care settings. For example, more recently orthoptists have become involved in diabetic retinopathy screening and grading, and in glaucoma shared-care schemes.[7-10] In relation to nAMD, orthoptists are increasingly involved in making recommendations for anti-VEGF treatment particularly on the basis of the OCT assessment.

To the authors' knowledge, the rate of agreement between orthoptists and ophthalmologists in making a treatment decision based on OCT interpretation has yet to be investigated. Previous studies have examined inter-observer agreement for detection of nAMD features on OCT scans,[6,11] OCT grading reproducibility in nAMD clinical research trials[12] and inter-grader consensus between the spectral- and time-domain OCT.[13,14] Most of these studies have involved certified trained readers from international reading centres interpreting the OCT scans. The aim of this study was to determine the rate of agreement between five orthoptists and an ophthalmologist working in a private ophthalmology practice in deciding whether anti-VEGF treatment for nAMD is indicated based on the interpretation of OCT images.

MATERIALS AND METHODS

Participants

A retrospective clinical audit was conducted at a private ophthalmology clinic in Melbourne, Australia. Data was collected from existing data reserves at the clinical practice during nAMD sessions conducted between the 8th April and 3rd September 2013. Three groups of data were collected: i) patient demographics, ii) clinical assessment details, and iii) the treatment decisions of five orthoptists and one senior vitreoretinal ophthalmologist based on the interpretation of the OCT images (Table 1). Each OCT image was reviewed by one of the five orthoptists and the ophthalmologist. At the time of data collection, the mean years of experience of the orthoptists was 3.61 years (range 1 to 4 years). All orthoptists routinely reviewed nAMD patients and received no additional specific training in OCT interpretation for the purposes of this study. The senior ophthalmologist had over 30 years experience in the investigation and management of posterior segment disorders and as such, their clinical decision making skills/treatment decisions were utilised as the 'gold standard' in this study.

Table 1. Data variables collected for clinical audit

Data Collected	Description
Patient demographics	• Gender • Date of consultation • Treated eye/s
Clinical assessment	
Distance BCVA (LogMAR, number of letters correct)	• Right eye • Left eye
OCT (Spectralis, Heidelberg Engineering)	• Central retinal thickness (CRT) • Maximum retinal thickness • Pigment epithelial detachment (PED)
Treatment decision	
Orthoptist	• No treatment • Injection required
Ophthalmologist	• No treatment • Injection required
Agreement between the orthoptists and ophthalmologist	• Agreement • Disagreement (with reasons/ ophthalmologist's clinical notes)

Procedures

Each patient attending the nAMD clinic during the study period underwent a routine clinical examination, including visual acuity testing and OCT imaging. The orthoptist was aware of the patient's acuity prior to OCT imaging. Best corrected visual acuity (BCVA) was assessed by the orthoptist using a retro-illuminated Early Treatment of Diabetic Retinopathy Study (ETDRS) chart at 3 metres and recorded as the number of letters read correctly. A value of zero (0) was recorded if the BCVA was no perception of light (NPL), light perception (PL), hand movements (HMs) or count fingers (CFs). An orthoptist also performed the OCT scan for each patient. All OCT images were acquired using the same Spectralis HRA+OCT machine (Heidelberg Engineering, Heidelberg, Germany) and measurements of central retinal thickness (CRT), maximum retinal thickness and pigment epithelial detachment (PED) were recorded in micromillimetres (μm). After acquiring the OCT scan, the orthoptist indicated in writing on the patient file if they recommended an injection based on the appearance of the scan. The treating ophthalmologist then independently reviewed the OCT scan and recorded their treatment decision on the same patient file. Treatment decision was primarily based on the level of disease activity evident on OCT scanning, whereby areas of hyporeflectivity represent the presence of fluid and indicate the need for intravitreal injection. This treatment regime is classified as *pro re nata* methodology, that is, a patient receives treatment when needed, as opposed to the more commonly used regime for anti-VEGF treatment known as 'treat and extend'. In instances where the ophthalmologist's treatment decision was not solely based on OCT appearance, the ophthalmologist included written commentary in the patient's file as to the additional factors influencing their treatment decision. For all cases where there was disagreement between the treatment decision of the orthoptist and that of the ophthalmologist, the relevant OCT scans were retrieved by the study investigators to investigate the possible reason(s) for disagreement.

Data Analysis

An analysis of the inter-rater agreement between the five orthoptists and the treating ophthalmologist (all orthoptists versus ophthalmologist) was performed using the kappa statistic. The kappa statistic was interpreted in line with the ranges suggested by Landis and Koch,[15] where a kappa of: 0.81 - 1.00 = near perfect agreement; 0.61 - 0.80 = substantial agreement; 0.41 - 0.60 = good agreement; 0.21 - 0.40 = fair agreement; 0.10 - 0.20 = slight agreement; and 0 = poor agreement. The SPSS statistical program (IBM SPSS Statistics 21.0) was used for calculations.

RESULTS

Participants

A statistical power calculation conducted a priori showed that a minimum sample size of 635 eyes was required to detect a statistically significant result, where the minimum acceptable value of kappa was 0.70 and the ideal kappa to detect was 0.80, with power set at 90% and $p \leq 0.05$, two-tailed. A total of 669 eyes were included in this clinical audit. This consisted of 402 individual patients, with 267 patients having nAMD in both eyes.

There were 443 eyes of female patients (66%) and 226 eyes of male patients (34%). Right and left eyes were almost equally represented (RE 50.8%, LE 49.2%). The mean BCVA was 64.5 letters (range 0 to 91; SD ± 17.69) and 63.9 letters (range 0 to 90; SD ± 18.83), in the right and left eyes respectively, approximately equivalent to 6/15 Snellen acuity. The measurements of CRT, maximum retinal thickness and PED for the right and left eyes are shown in Table 2.

Table 2. Central retinal thickness, maximum retinal thickness and pigment epithelial detachment

Measurement (μm)	Right eye Mean (SD)	Left eye Mean (SD)
Central retinal thickness (CRT)	262.49 (126.69)	261.42 (120.29)
Maximum retinal thickness	423.87 (125.74)	415.58 (118.64)
Pigment epithelial detachment (PED)	198.67 (126.79)	187.56 (112.02)

Inter-rater agreement between orthoptists and ophthalmologist

Of a total 669 treatment decisions made, there were 619 agreements between the orthoptists and the ophthalmologist. This was equivalent to an agreement rate of 92.5%. Conversely, on 50 occasions, the treatment decision of the orthoptist differed to that of the ophthalmologist. This was equivalent to a disagreement rate of 7.5%. The pattern of agreement and disagreement is shown in Table 3, with an almost equal proportion of disagreement between the decision of injection or no injection. The inter-rater agreement between the orthoptists and the ophthalmologist in making a treatment decision based on OCT interpretation was found to be $\kappa = 0.85$ (95%CI 3.434 - 1.258, $p < 0.001$), representing an almost perfect agreement.[15]

Table 3. Treatment decision by orthoptists compared with ophthalmologist (N = 669)

	Ophthalmologist: Injection needed	Ophthalmologist: Injection not needed
Orthoptist: Injection needed	280	26
Orthoptist: Injection not needed	24	339

The 50 disagreements were investigated for possible reason(s) contributing to the difference in treatment decision. The clinical notes of the ophthalmologist (where available) were the first source of information when investigating the reason(s) for disagreement. The OCT scans were also retrieved by the study investigators. In a large proportion of cases where there was disagreement between the orthoptist and ophthalmologist, the patient's OCT scan showed stability of the disease but the ophthalmologist had indicated that it was safer to inject to prevent disease re-activity/fluid return with no additional commentary provided. Other reasons included subtle disease activity (slight subretinal fluid or slight macular oedema), or the patient was going on vacation and/or unable to attend a future scheduled visit so it was considered necessary to administer treatment at the present visit. On occasions where the orthoptist had indicated an injection was required but no injection was administered by the ophthalmologist, the main reason for the discrepancy was that the disease state was considered stable by the ophthalmologist and as such, no treatment was administered.

DISCUSSION

OCT imaging is gaining increasing recognition as a valuable tool in the diagnosis and monitoring of disease progression in patients with nAMD. In particular, OCT interpretation forms a critical part of the treatment decision-making process in patients with nAMD. Currently, this task is predominantly performed by the treating ophthalmologist. However, the increasing prevalence of nAMD due to an ageing population is likely to translate into greater demand for eye care services in the future. In Australia, the orthoptic scope of practice has expanded over the past few decades in response to heightened service capacity pressures, with orthoptists assuming greater responsibility in the management of glaucoma patients[1] and becoming increasingly involved in paediatric triaging[7,9,16] and diabetic screening.[6] The inter-rater consensus between orthoptists and ophthalmologists is of considerable interest as orthoptist-led AMD screening/monitoring clinics represent a potential means of addressing the increased burden on the healthcare system.

This study has been the first to investigate the agreement rate between orthoptists and an ophthalmologist in making a clinical decision as to whether anti-VEGF treatment for nAMD is indicated based on OCT interpretation and has found a near perfect agreement. Where there was disagreement, the patients were not placed at sight-threatening risk.

Previous studies have likewise reported relatively high inter-observer agreement for the grading of nAMD features on OCT scans.[6,11-13] The high inter-rater agreement value in the current study could be partially attributed to the use of highly trained orthoptists. Orthoptists involved in this study were recent graduates from La Trobe University where there is a significant focus on the diagnosis and management of ophthalmic disease as well as ocular motility disorders and were routinely working on a clinic dedicated to AMD patients. Another factor which may have contributed to the high agreement rate observed was the use of spectral-domain OCT. All images acquired in this study were obtained using a Spectralis HRA+OCT machine. OCT device-type can influence clinical interpretation of OCT imaging in the context of nAMD.[13,14] Spectral-domain OCT systems have been found to generate a higher degree of inter-rater consensus than time-domain OCT systems when judging scans for the presence of intraretinal and subretinal fluid,[13,14] and epiretinal membranes.[15] Whilst a limitation of these studies was that they only included a small number of independent graders,[3] their findings suggest that the choice of spectral-domain versus time-domain OCT systems can impact clinical decision-making in nAMD.

A healthcare model utilising shared-care management of AMD could address the growing demand for eye care. Introducing orthoptist-led AMD screening and monitoring clinics may produce greater efficiency by reducing waiting times for patients and increasing capacity within specialist clinics.

In summary, this study revealed an almost perfect agreement between orthoptists and an ophthalmologist in making treatment decisions for nAMD patients based on OCT interpretation. These early results, in conjunction with those of other studies, lend support to the expanding role of orthoptists and the development of orthoptist-led clinics for screening/monitoring patients with AMD. With the growing ageing population, increasing the orthoptic scope of practice represents a potential solution to ease the burden of chronic eye diseases on the healthcare system. However, it is important to acknowledge that this retrospective review was confined to only one private ophthalmology clinic and data was collected from a small sample of orthoptists and only one ophthalmologist. The inclusion of only one ophthalmologist limits the capacity to identify if there are differences in management decisions between ophthalmologists. For instance, it is likely that some ophthalmologists may have elected not to inject where the nAMD was stable, when the *pro re nata* regime is used. Furthermore, the ophthalmologist was not masked to the treatment decision made by the orthoptists. Thus, additional studies conducted across a variety of different hospital and clinical settings that involve a larger number of raters, all of whom are blind to the treatment decision of other raters, are required to confirm these findings.

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