Correlation between Ocular Surface Disease Index and tear meniscus height in dry eye disease

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Abstract

Background: Dry eye disease is a common and potentially vision-threatening problem. The Ocular Surface Disease Index (OSDI) is a well-established method of subjectively assessing dry eye disease. Objective means of diagnosing dry eye disease suffer from poor reproducibility, low sensitivity and specificity, are invasive, time consuming and often require specialised equipment. It is hypothesised that optical coherence tomography (OCT) of the tear meniscus may address these problems.

The primary aim of this study was to describe the correlation between the OSDI and tear meniscus height (TMH) in dry eye disease measured by OCT. The secondary aim was to determine a useful diagnostic cut-off value for TMH in the diagnosis of dry eye disease. The study was conducted at St John Eye Hospital – a tertiary hospital in Johannesburg, Soweto, South Africa.

Methods: This was a prospective, cross-sectional study of adults at a tertiary level eye clinic. Participants were included if they were older than 18 years, and excluded if they were contact lens wearers, had an established diagnosis of dry eye disease, or were known to have (or be taking any treatment for) any ophthalmological or medical condition that has the potential to influence dry eye disease. A control and investigative group was determined using the dry eye OSDI. The inferior TMH of both groups was imaged using OCT.

Results: A total of 36 right eyes of 36 patients were included in this study. Patient ages ranged from 20–64 years, with a median age of 43 years. Overall, there were more females (n=27) than males (n=9). There was a moderate negative correlation between the normal/dry eye group and TMH (r=-0.452, p=0.032). Optimising sensitivity and specificity yielded a diagnostic cut-off TMH of 296 um.

Conclusion: Tear meniscus height tends to decrease between OSDI classifications of ‘normal’ and ‘dry eye disease’. However, TMH performed poorly as an objective measure of dry eye disease in our study population, limiting recommendations to adopt it as a diagnostic test.

Keywords: dry eye disease, Ocular Surface Disease Index, optical coherence tomography, tear meniscus height

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Introduction

Dry eye disease is a common problem with an estimated one in four patients presenting to eye clinics with characteristic symptoms, and a global prevalence of 7–34%. There is a paucity of epidemiological data for South Africa and indeed the African continent with an estimated prevalence of 41–92% in...
three small population-based studies.\textsuperscript{3–7} Furthermore, dry eye disease results in a significant economic burden, with an average expenditure of USD $11 302 per patient and a total of USD $55.4 billion yearly in the United States of America alone.\textsuperscript{8}

There are a number of well-validated questionnaires that have been developed to subjectively assess dry eye disease – the Ocular Surface Disease Index\textsuperscript{6} (OSDI) is one of the most frequently used and performs well with a sensitivity and specificity of 60% and 83% respectively.\textsuperscript{9,10} The OSDI consists of 12 questions based on the recall of symptoms in the preceding week. Severity, environmental factors and the degree to which activities of daily living are affected are all scored.

In contrast there is no gold standard objective measurement to quantify or monitor dry eye disease. Schirmer’s test, ocular surface staining, fluorophotometry, biomarker sampling and osmolarity are invasive, suffer from inaccuracy or poor reproducibility, are time consuming or require specialised equipment that may not be readily available in the clinic setting.\textsuperscript{11,12}

Non-invasive methods are attractive as they do not induce reflex tearing which may increase the normal rate of tear secretion by 100–500%.\textsuperscript{13} This, combined with recent advances in anterior segment optical coherence tomography (AS-OCT), has renewed interest in meniscometry as means of measuring tear volume as a proxy for dry eye disease.\textsuperscript{14–16} Experimental studies have shown that the inferior tear meniscus, which is formed in the angle between the cornea and the lower lid (Figure 1), compromises 75–90% of total tear volume. Within this, the tear meniscus height (TMH) varies little in absolute value terms from tear meniscus area and performs the best diagnostically in both specificity and sensitivity in predicting disease.\textsuperscript{14–16}

The primary aim of our study was to describe the correlation of TMH against the OSDI. Additionally, we aim to determine a diagnostic cut-off of TMH for diagnosing dry eye disease.

Methods

This was a prospective, cross-sectional, case-controlled study conducted at St John Eye Hospital, Soweto, Johannesburg, South Africa. Ethical clearance was approved by the Human Research Ethics Committee, University of the Witwatersrand (M190650). The study was conducted in accordance with the declaration of Helsinki.

A sample size of 20 (17±10%) for each group was determined using anticipated mean differences; a \( p \)-value of <0.05 was taken to be significant. Considering the strict exclusion criteria and the anticipated difficulty in recruiting participants, especially to the control group, we decided not to power the study to perform a sub-group analysis of severity of disease, age or sex.

Patients, their family members or escorts, and staff members older than 18 years were randomly recruited to be invited to participate in the study. Participants were excluded if they were current contact lens wearers, had used topical eye drops in the preceding 14 days or had undergone any previous intraocular or extraocular surgery including laser and refractive procedures. Patients were also excluded if they were pregnant or lactating; or if they had a systemic disease or were using treatments for: diabetes mellitus, thyroid disease, Sjögrens syndrome, hepatitis C, vitamin A deficiency, human immunodeficiency virus (HIV) infection or any hormonal dysfunction.\textsuperscript{17,18} Patients were also excluded if they were unable to speak English, Afrikaans, Zulu or Sotho.

A brief direct ophthalmoscope examination was performed to exclude localised ocular pathology such as blepharitis, pterygium and pinguecula. Demographic data including the participants’ age, sex and race was collected. In addition, the total duration of dry eye symptoms was captured (if applicable). Each participant was divided into a control (‘normal’) or investigative (‘dry eye disease’) group based on the recall of symptoms of dry eye in the preceding week using the dry eye OSDI iOS application (Allergan Inc., Dublin, Ireland). The investigative group was further divided into ‘mild’, ‘moderate’ and ‘severe’.

Each group’s TMH was measured using a SPECTRALIS\textsuperscript{®} (Heidelberg Engineering, Heidelberg, Germany) OCT with anterior segment capabilities. A light source 1 310 nm wavelength, 60 nm bandwidth, scan width 15 mm at eight frames per seconds, scan depth 2 mm in air and optical resolution less than 10 um was set. Measurements were taken in a dimly

Figure 1: (A) Lower lid tear meniscus shown together with infrared photo of the lower cornea and lid (frame); (B) Tear meniscus height (TMH) and tear meniscus depth (TMD); (C) Tear meniscus angle and angle alpha (\( \alpha \))\textsuperscript{19,20}
lit room from 10.00 to 16.00 during the months of November 2019 to March 2020. Each participant was asked to blink and then maintain central and steady gaze while three scans were taken approximately two seconds later. The anatomical landmark was taken to be the midpoint of the lower lid in primary gaze. Each scan was manually inspected and a quality index of greater than 20 was taken as sufficient. The TMH was measured in each scan using the caliper function at a standard magnification of 3× and averaged to mitigate random error.

Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) software (IBM Corp. Released 2016. IBM SPSS Statistics for Mac, Version 24.0 Armonk, NY: IBM Corp.)

Results

Patient characteristics

A total of 36 right eyes from 36 patients were included for analysis. Shen et al. showed that dry eye disease is bilateral and equally affects each eye; thus, the right eye was chosen by convention. Participant age ranged from 20–64 years, with a mean of 43 years (95% confidence interval, 39.3–46.7). The age group 41–50 years accounted for 39% of all participants. Overall, there were more females (n=27) than males (n=9). All the participants were black Africans. The mean duration of dry eye symptoms was 428 days, the median was 56 days with a range of 0–3 640 days, standard deviation 880 days. Within the ‘dry eye disease’ group, 55% were classified as mild, 13.6% as moderate and 36.4% as severe. Table I shows a breakdown of the control and investigative groups according to sex and age demographics.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Control (n=14)</th>
<th>Dry eye disease (n=22)</th>
</tr>
</thead>
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<td>7</td>
</tr>
<tr>
<td>Female</td>
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<td>15</td>
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<tr>
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Correlation analysis

A Pearson correlation coefficient revealed a weakly negative relationship between raw OSDI scores and TMH (r=−0.211, p=0.216) as shown in Figure 2. However, a bi-serial analysis performed by examining only ‘normal’ and ‘dry eye disease’ as a function of TMH showed a more strongly negative, significant relationship (r$_b$=−0.452, p=0.032). A variance analysis showed that TMH contributed only 4.45% to the overall variance observed in OSDI scores.

There was no correlation between the duration of symptoms and TMH (r=−0.066, p=0.702).

An independent t test of TMH in isolation revealed that it was indeed higher in the control group (M=659 um, SD=676 um) compared to the investigative group (M=325 um, SD=173 um); however, this was not found to be statistically significant (p=0.092).

Diagnostic cut-off for TMH

A diagnostic cut-off for determining ‘normal’ from ‘dry eye disease’ participants was determined by linear regression analysis of receiver operating curves (ROC) as shown in Figure 3.

Choosing a TMH which optimises sensitivity and specificity (50% and 36% respectively) yields a TMH of 296 um. Maximising sensitivity at the cost of specificity (77% and 7% respectively) yields a diagnostic cut-off of 224 um. The area under the curve (AUC) is 0.289, indicating an overall poor diagnostic performance.

Power and effect size

Our study had a Cohen effect size of 0.4 indicating a small-to-medium effect size. Retrospective calculation of a larger effect using our available data (>0.8) would have required 36 participants in each group for a total of 72.

Discussion

Dry eye disease is a common problem and invasive methods of assessment are currently unsatisfactory. AS-OCT TMH has shown promise as a non-invasive diagnostic test that addresses these problems.

To the best of our knowledge this is the first study of its kind in South Africa attempting to compare TMH against a validated method such as the OSDI. Our study found that TMH tends to decrease in those whose symptoms are sufficiently severe to have been classified as dry eye disease by the OSDI. This is consistent with the findings of other studies and may be explained by the fact that in the absence of reflex tearing, the volume of tears is lower than in control subjects.22,13,18 It is important to note that dry eye disease incidence
increases with increasing age, affecting females within this population more than men, reflecting decreased hormonal-mediated components of tear production. The tear film consists of a proportionally large volume of aqueous sandwiched between an outer lipid layer and an inner mucinous layer. Regardless of whether the dry eye state is as a result of aqueous deficiency or an accelerated evaporative state, the aqueous is reduced.¹

There is no consensus regarding a diagnostic cut-off value for TMH in dry eye disease. Shen et al.¹⁵ suggested a value of 164 um with an associated sensitivity and specificity of 92% and 90% respectively, while Tung et al.¹⁶ calculated 210 um as their value. Yet another group, Ibrahim et al.,¹⁷ found a higher value <300 um to be statistically significant. Our study concluded that 296 um was the point at which one could maximise diagnostic power (sensitivity 50%, specificity 36%). However, since this test is intended primarily for screening purposes, it is reasonable to maximise the sensitivity which yielded a cut-off of 224 um and a sensitivity and specificity of 77% and 7% respectively. While the absolute value and sensitivity of this value is similar to other authors’ findings, our specificity and overall diagnostic power was considerably lower, which limits the recommendation that this should be adopted as a diagnostic tool in our population.¹³,¹⁵,¹⁶ This may reflect a limitation in our study or an undescribed intrinsic difference in our population, the description of which exceeds the scope of this study.

Our study was limited by a small sample size although it is noted that similar studies included both left and right eyes for analysis which may enhance a statistical effect. A single unmasked investigator used clinical judgement to measure the TMH which may have introduced unintended bias. It was not possible to control for all factors which may influence the tear meniscus such as palpebral aperture height, corneal curvature and ambient conditions.

Future well-designed studies should attempt to recruit a larger participant pool and sufficiently power their statistical analysis to include sub-groups such as age, sex and OSDI severity. It may be necessary to develop automated software techniques that are able to determine tear meniscus variables with a high degree of accuracy.

### Conclusion

Dry eye disease is commonly encountered and potentially vision-threatening, but despite this, there is little evidence about the prevalence locally or more widely on the African continent.

While recall questionnaires such as the OSDI are well-validated, objective non-invasive methods of diagnosis are lacking.

AS-OCT meniscometry is a potential alternative to this problem that has shown promise in international studies. We have shown that TMH tends to decrease in dry eye sufferers compared to those without symptoms as validated by the OSDI, but this relationship has neither the same robustness nor diagnostic value as described in similar studies. This could reflect inherent limitations in our study or a broader difference in our local populace that needs to be further elucidated. As such TMH meniscometry should not be used as a diagnostic tool, or used with caution, in our local population.

### What was known:

- Subjective methods of diagnosing dry eye disease such as the OSDI are useful and well validated.
- TMH as measured by AS-OCT shows promise as an objective tool in diagnosing dry eye disease in international studies.

### What this article adds:

- It confirms that TMH tends to decrease with increasing symptoms of dry eye disease.
- TMH performs poorly as a diagnostic test in an isolated South African population.

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### References