Upper and Lower Tear Menisci in the Diagnosis of Dry Eye

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PURPOSE. To measure the upper and lower tear menisci in patients with aqueous tear deficiency (ATD) dry eye by real-time optical coherence tomography (OCT) and to determine the most effective meniscus variables for the diagnosis of dry eye.

METHODS. Eyes of 48 pre-screened ATD patients were compared with those of 47 healthy subjects. Upper and lower tear menisci were imaged simultaneously by real-time OCT immediately after blinking. The height, radius, and cross-sectional area of upper and lower tear menisci were obtained.

RESULTS. The tear meniscus radius, height, and cross-sectional area were significantly smaller in patients with dry eye than in healthy subjects (P < 0.01). The lower tear meniscus variables were higher than the upper meniscus (P < 0.01) in normal subjects; however, no significant differences between menisci were found in ATD patients. In both groups, the upper and lower tear meniscus variables were strongly correlated with each other. Good dry eye diagnostic accuracies were obtained with cutoff values for an abnormal lower tear meniscus radius (LTMR) of 182 μm and a lower tear meniscus height (LTMH) of 164 μm. The LTMR diagnostic sensitivity and specificity were 0.92 and 0.87, respectively. The LTMH diagnostic sensitivity and specificity were 0.92 and 0.90.

CONCLUSIONS. Upper tear meniscus variables in ATD patients were assessed by real-time OCT. The tear meniscus was smaller in ATD patients than in healthy subjects. LTMR and LTMH may have potential in the diagnosis of ATD. (Invest Ophthalmol Vis Sci. 2009;50:2722–2726) DOI:10.1167/iovs.08-2704

Normal tear volume is important for the maintenance of ocular surface physiology and ocular comfort. The total tear volume is composed of the tear meniscus, which contains 75% to 90% of the tears; the pre-ocular film; and the cul-de-sac. Small tear volumes may result in dry eye symptoms, especially in aqueous tear deficiency (ATD). However, measuring the actual tear volume is difficult because the methods are invasive and irritative. Reflex tear production can be induced, giving an overestimation of basal tear flow and volume. The sizes of the tear menisci are related to the tear secretion rate and tear stability, and they are good indicators of the overall tear volume. The tear menisci are decreased in ATD patients, and measurement of the menisci may serve as a diagnostic tool. Estimates of menisci size and volume have been attempted by photographic and interferometry methods. However, these methods do not allow the simultaneous imaging of both the upper and lower menisci. Recent advances in optical coherence tomography (OCT) and associated software have enabled the simultaneous imaging of both menisci, and real-time changes have been reported. OCT-derived quantitative measurement of tear meniscus variables enable this noninvasive modality as a potential diagnostic tool of dry eye. The purpose of this study was to measure the upper and lower tear menisci in ATD patients and control subjects to determine which of the variables are most effective in the diagnosis of dry eyes.

METHODS

This research was conducted in strict accordance with the guidelines of the Wenzhou Medical College Review Board, Wenzhou, Zhejiang, China, and in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject after a full explanation of the procedures. Both eyes of 48 ATD patients were studied. The group included 34 women and 14 men with a mean age of 38.6 ± 13.2 years (±SD; range, 18–74). A group of 47 healthy persons of similar age distribution was recruited from students and faculty in the Wenzhou Medical College. This group included 24 women and 23 men with a mean age of 38.5 ± 12.7 years (range, 18–75). They were considered healthy if they had no history of ocular irritation and had a Schirmer I test score of more than 5 mm. Subjects with a history of conjunctivitis, scleral, or corneal diseases, previous eye surgery, glaucoma, diabetes mellitus, thyroid disorders, antidepressant or diuretic medication, or contact lens wear were excluded from both groups.

Patients presenting with complaints of ocular irritation were evaluated by a clinical ophthalmologist (HM) at the Ocular Surface Service, Eye Hospital, Wenzhou Medical College. On the day before OCT imaging, each patient or control subject was first asked to complete the McMonnies dry eye survey and then underwent Schirmer I testing and slit lamp biomicroscopy to evaluate the lid margins, meibomian glands, and height of the inferior tear meniscus. Based on the results of these tests, ATD was diagnosed if the patient had bilateral Schirmer I test results of 5 mm or less, bilateral inferior tear meniscus height of less than 0.1 mm, as observed by slit lamp biomicroscopy and 3 one or more of the McMonnies survey primary dry eye symptoms occurring at least occasionally.

Measurement of Upper and Lower Tear Menisci with Real-Time OCT

The real-time OCT instrument for this study was described by us previously, and a similar system can be found in other studies. The OCT system light source had a 1510 nm wavelength with 60 nm bandwidth, the scan width was up to 15 mm at eight frames per second, the scan depth was set at 2 mm in air, and the optical

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resolution was less than 10 μm. The source was mounted on a standard slit lamp with a probe that was connected to a telecentric light-delivery system. For the tear meniscus image, the patient was asked to stare at an external target. The images were recorded when a clear reflection of the central cornea was obtained on a monitor. The cross-sectional images simultaneously included the upper and lower tear menisci.

**Procedure**

All subjects were tested between 10 AM and 4 PM in a dimly lit consulting room where the temperature (15–25°C) and humidity (30%–50%) were controlled with air conditioning and a dehumidifier. All subjects were told not to use eye drops within 1 hour before consulting the laboratory for the study. The same examiner (JL) performed all tests. Both eyes of each subject were imaged by real-time OCT. One eye was randomly selected to be tested first, and testing of the companion eye followed. Both upper and lower tear meniscus measurements were obtained immediately after normal blinking.

The imaging process to obtain tear meniscus variables was described in a previous study. Briefly, the first good image showing both upper and lower tear menisci taken immediately after a blink was used. To process the image, operator inputs were provided to identify three touch points used to fit a circle that yielded the tear meniscus curvature. Two of these three points included the locations where the tear surface touches the cornea and the lids. The third touch point was the middle of the front edge of the meniscus on the ocular surface. Upper tear meniscus radius of curvature (UTMR), upper tear meniscus height (UTMH), upper tear meniscus cross-sectional area (UTMA), lower tear meniscus radius of curvature (LTMR), lower tear meniscus height (LTMH), and lower tear meniscus cross-sectional area (LTMA) were obtained.

**Statistical Analysis**

All data are presented as the mean ± SD. Independent sample *t*-tests were applied to the comparison of tear menisci parameters between ATD patients and normal control subjects. Paired sample *t*-tests were used to compare the differences between upper and lower tear menisci in each group. A level of *P* < 0.05 was accepted as statistically significant. Diagnostic variables for ATD were analyzed by receiver operating characteristics (ROC) curves, and the areas under the ROC curves (AUC) were compared. To construct the ROC curves, the sensitivity, measured as the proportion of ATD patients who were positive for the variable, and the specificity, measured as the proportion of healthy subjects who were negative for the variable, was calculated (SPSS version 13.0 for Windows XP; SPSS Inc., Chicago, IL).

**Results**

There were no significant differences between left and right eyes within each group respectively (paired sample *t*-test, *P* > 0.05). The radius, height, and cross-sectional area of the upper and lower tear menisci in the ATD eyes were significantly smaller than the comparable variables in normal eyes (independent sample *t*-test, *P* < 0.01, Table 1, Fig. 1). For both groups, the radius, height, and area of the upper meniscus were linearly correlated with the same variables in the lower menisci (*r* = 0.425–0.497, *P* < 0.01 for each variable). Further, in control subjects, the lower tear meniscus variables were all greater than the upper meniscus (paired sample *t*-test, *P* < 0.01); however, there were no significant differences between the upper and lower tear meniscus variables in the ATD group (paired sample *t*-test, *P* > 0.05, Table 1, Fig. 2). In both the ATD and control groups, the Schirmer I test correlated significantly with the variables of the lower tear meniscus (*r* = 0.21–0.34, *P* < 0.01). It also correlated with UTMA in control subjects. *Results from dry eye patients (n = 48) were significantly lower than those for normal subjects (n = 47) for each of the measured variables (P < 0.01).*
Comparison of tear meniscus variables. There were no differences in the radius (A), height (B), and area (C) between left and right eyes within each group (paired sample t-test, \( P > 0.05 \)). The upper tear meniscus variables were significantly smaller than the lower tear meniscus for eyes in the control group (paired sample t-test, \( P < 0.01 \)). However, there were no significant differences between the upper and lower menisci variables within the ATD group (paired sample t-test, \( P > 0.05 \)).

AUCs of ROC curves can vary between 0 and 1, with larger values indicating greater sensitivity and specificity. The individual AUCs of the six variables of the upper and lower tear menisci calculated by the ROC technique ranged from 0.78 to 0.95. After the upper and lower tear menisci radii, heights, and areas were combined, the AUCs were 0.94, 0.94, and 0.87, respectively, suggesting reliable sensitivity and specificity of the OCT tests (Table 2, Fig. 3). The cutoff value, derived from each ROC curve, is the point with an optimal relationship between sensitivity and specificity. Among the upper and lower tear meniscus variables analyzed, LTMR and LTMH had the largest AUCs, both 0.95. With cutoff values for abnormal LTMR and LTMH of 182 and 164 \( \mu \text{m} \), respectively, good diagnostic accuracies were obtained. For LTMR, the sensitivity was 0.92 and the specificity was 0.87 (Table 2). For LTMH, they were 0.92 and 0.90, respectively.

**DISCUSSION**

Similar to others,\(^6\)\(^-\)\(^23\)\(^,\)\(^24\) we found that all the tear menisci variables were significantly lower in ATD patients compared with normal subjects. Using noninvasive interference tear meniscometry, Uchida et al.\(^{13}\) reported that the mean lower tear meniscus height was significantly smaller in ATD patients with Sjögren’s syndrome than that in the control group. Our values for LTMR are in agreement with that obtained by them and by posterior segment OCT.\(^{15}\) When measured by video meniscometry,\(^{12}\) reflective meniscometry,\(^{25}\) and by fluorescein photography,\(^5\) meniscus heights and radii are greater than in our study. OCT measurements are noninvasive and induce little or no reflex tearing, which may explain the discrepancies between some of our findings and those with fluorescein and visual light that can induce reflex tearing. Similar to our previous study that was also conducted in Chinese subjects,\(^{17}\) we noticed that the normal lower tear meniscus was greater than the upper tear meniscus. This anatomy is different from that in a previous study conducted in the United States in which the upper and lower tear menisci were similar to one another.\(^{21}\) The differences can be attributed to the different characterizations of eyelids, as discussed in the field of blepharoplasty for Asians.\(^{26}\) Tight eyelids and the narrow apertures may play a role in holding tears around the upper eyelids in Chinese eyes. We also found the relationship between Schirmer I test and OCT results of the lower tear meniscus in both groups, which is not in agreement with our previous study conducted in the United States.\(^{21}\) In our previous study,\(^{21}\) the Schirmer II test was used and the results did not significantly relate to OCT results of tear menisci in normal subjects. Different populations between the previous and present studies may also contribute to the disagreement.

Tear distribution between the upper and lower tear menisci appears to be dependent on tear volume. The upper tear meniscus was significantly smaller than the lower one in control subjects. In contrast, there were no significant differences between the upper and lower menisci variables in ATD patients. This change in relative distribution was due to the greater decrease in the lower meniscus than the upper meniscus in ATD patients. Tear distribution on the ocular surface may be affected by multiple factors, including surface tension, gravity, capillary effect, and structural limitations that hold tears. With a larger volume on the ocular surface, gravity may play a major role in the tear distribution. In the normal group, the upper meniscus filled out fully, and the excess tears were distributed to the lower tear meniscus. This finding was reported previously by Wang et al.\(^{27}\) After the instillation of artificial tears, the difference between the upper and lower tear menisci gradually became greater. There might be some limit to the capacity of the upper tear meniscus that causes it to stop increasing with the increased volume of the tear film. Of interest, there was a strong correlation between upper and lower tear menisci in the ATD group, suggesting that both may be affected by low tear volume. Thus, the evaluations of both upper and lower tear menisci are important for the diagnosis of ATD.

The traditional objective diagnosis of dry eye in the clinical setting relies on the Schirmer test, break-up time, and vital
staining of the ocular surface. These invasive tests may cause irritation and reflex tearing and can influence the results. Often the information gained from each test is not consistent with the others. The efficacy of several tests for the diagnosis of dry eye, both singly and in combination, has been reported by other investigators.28–30 Khanal et al.28 assessed specific tests, including tear quality, evaporation, turnover, volume, and osmolarity, to optimize the diagnosis of dry eye in a range of dry eye conditions. They documented that tear osmolarity is the most appropriate individual diagnostic test for dry eye, whereas the combination of tear turnover rate, evaporation, and osmolarity is the most suitable battery of tests. They also showed that tear turnover rate was the best method to discriminate between ATD and other types of dry eye. However, tear volume in that study was determined by Schirmer’s test. It is probable that the invasive nature of that test led to an overestimation of tear volume and a reduction in sensitivity as a diagnostic tool. The highest accuracy for dry eye diagnosis in the literature appears to be the quantitation of tear lysozyme.29

However, some patients with severe dry eye were included in that study and efficacy of the test may be influenced by selection bias.

On the basis of our results, LTMR and LTMH showed good diagnostic accuracy with more than 0.87 both for specificity and sensitivity in the diagnosis of ATD. Similar results were found in a previous study.3 Thus, the lower tear meniscus variables are more sensitive and specific than those for the upper tear meniscus. The ROC curves in our study support this notion. The combination of upper and lower tear meniscus variables data results in an accuracy that is at least equal to or better than the individual accuracies. Because of the relatively small sample size in this study, these results should be confirmed in a large clinical trial before they can be used with confidence to diagnose ATD. In addition, it should be noted that the diagnostic efficacy in this study may have been affected by selection bias. The ATD patients were pre-screened by Schirmer’s test (<5 mm). Thus, some ATD patients may have been excluded because of the unreliable nature of this test.

There are some limitations in the present study. First, the palpebral aperture and blink rate varied in the different subjects, and the differences may have had an effect on tear meniscus variables. We did not control palpebral aperture and blink rate, and the subjects were asked to open their eyes in a natural way and blink spontaneously. Second, to process the images, the operator used his own judgment to locate the junctions of the tear meniscus points for the determination of the tear meniscus borders. Because the person who did the image processing was not masked on patients, some bias may have been introduced. Removing the potential for the bias and errors in judgment would necessitate development of automated image processing software to detect the tear meniscus height, radius, and area automatically. Third, the ATD patients varied widely in age. Thus, further studies on tear meniscus variables in different age groups and with other subtypes of dry eye are essential.

In conclusion, both tear menisci were decreased in ATD patients, and the sizes of the decreases were correlated with one another. LTMR and LTMH were the best indicators of ATD among the six tear meniscus variables measured. Measurements of tear menisci by OCT are rapid and noninvasive. They can provide valuable insight regarding the presence and therapeutic responsiveness of ATD and other forms of dry eye.

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