

Evaluation of Ocular Surface Epithelial and Stromal Thicknesses in Psoriasis Using Anterior Segment Optical Coherence Tomography

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Abstract

Purpose: To evaluate the epithelial and stromal thicknesses of conjunctiva and cornea in psoriatic patients with anterior segment optical coherence tomography (AS-OCT),

Methods: In this cross-sectional study, 61 patients with psoriasis and 42 age-matched, healthy individuals were enrolled. The epithelial and stromal thicknesses of both inferotemporal bulbar conjunctiva and central cornea were measured using AS-OCT.

Results: Both the Tear break-up time and Schirmer-1 test values were significantly lower in the psoriasis group compared with the controls ($p < 0.05$). The epithelial thickness of conjunctiva and cornea did not differ between psoriasis and control groups. ($p > 0.05$) The central corneal stroma was significantly thicker in the psoriasis group ($p = 0.04$). PASI was positively correlated with the thickness of central cornea stroma ($r = 0.442$, $p = 0.006$) in the nail psoriasis group.

Conclusions: Psoriasis is not associated with altered epithelial thicknesses of the cornea and conjunctiva. It is accompanied by the stromal thickening of the cornea without conjunctival stromal involvement.

Introduction

Psoriasis is a common chronic inflammatory skin disease that can show a variety of clinical manifestations. It is considered one of the most common immune-mediated disorders. Chronic plaque psoriasis, the most common subtype of psoriasis, is characterized by papulosquamous lesions. Psoriasis has also been defined as a multisystem chronic inflammatory disorder associated with multiple comorbidities. It is associated with many systemic disorders such as psoriatic arthritis, obesity, metabolic syndrome, hypertension, diabetes, and atherosclerotic disease [1]. Ocular manifestations are mostly asymptomatic or mildly symptomatic [2, 3]. Thus, the symptoms are underestimated by both the clinicians and the patients. Ocular manifestations were reported in up to 81.4% of psoriasis [4, 5]. Dry eye disease (DED) is one of the most common ocular manifestations of the psoriasis. Using Dry-Eye Questionnaire, Her et al. [6] reported 36.6% of the psoriatic patients experienced dry eye symptoms. The studies emphasizing dry eye related ocular surface alterations in psoriasis focused on the tear film changes [4, 6, 7], tear osmolarity [8, 9], conjunctival impression cytology [4, 6]. Using conjunctival impression cytology, Karabulut et al. [4] reported important cell alterations and squamous metaplasia in conjunctiva. Similarly, decreased goblet cell density and a high incidence of squamous metaplastic changes were observed [6].

The second site of involvement in ocular surface due to the inflammatory nature of psoriasis is cornea. Using the ocular response analyzer (ORA), statistically significant alterations of corneal biomechanical properties including corneal hysteresis (CH) [10] and corneal resistance factor (CRF) [10, 11] were observed. Moreover, Edris et al. [11] reported a negative correlation between CH and disease activity of psoriasis.

Currently, anterior segment optical coherence tomography (segment optical AS-OCT) enables clinicians to take cross-sectional thickness measurements of conjunctival and corneal layers are becoming more widely used in clinical studies. AS-OCT with the high capability to recognition of epithelium and stroma of conjunctiva and cornea could yield important insights into ocular surface involvements in psoriasis.

To the best of our knowledge, ocular surface epithelial and stromal thickness changes in psoriasis have not been reported previously. We hypothesized that psoriasis related infiltration of inflammatory cells and cytokines into the conjunctiva and cornea may drive changes of ocular stroma thicknesses. Furthermore, desiccating stress of poor quality of tear and the dry eye related inflammation may disturb the conjunctiva and cornea. Thus, the present study using AS-OCT was conducted to evaluate epithelial and stromal thicknesses of conjunctiva and cornea in patients with psoriasis

Methods

This prospective study was performed in accordance with the tenets of the Declaration of Helsinki and with the approval of the local ethics committee. We enrolled 61 patients with plaque psoriasis and 42 healthy controls. Informed consent was obtained from all individuals before participation. Patients younger than 18 years of age, with any systemic disease other than psoriasis

or ocular diseases such as hypermetropia exceeding 3 diopters (D), myopia and astigmatism exceeding 1 D, acute or chronic uveitis, keratoconus, glaucoma, nystagmus, and peripapillary chorioretinal atrophy, as well as patients undergoing ultraviolet phototherapy and anti-TNF- α therapy, those with any history of ocular trauma or surgery, or who were unable to cooperate while OCT measurements were being taken, were excluded from the study.

All participants underwent ophthalmic examinations, including best-corrected visual acuity, refractive error, intraocular pressure with a pneumatic tonometer (Auto Tonometer TX-F; Canon, New York), slit-lamp evaluation, tear breakup time (TBUT), Schirmer I test, extraocular movements, fundus examination, and conjunctiva and cornea thickness measurements with AS-OCT(Cirrus HD-OCT 4000; Carl Zeiss Meditec, Inc.).

The verification of plaque psoriasis was carried out by dermatological and histopathological evaluations. Medical records explored for duration of disease, joint and nail involvement, and medical treatments for psoriasis.

The psoriasis area and severity index (PASI) combining the severity (erythema, induration, and desquamation) and percentage of the affected area severity of psoriasis was used to represent the severity of psoriasis. Moreover, patients were divided into two groups based on nail involvement as the nail psoriasis is associated with a prolonged duration of psoriasis and greater severity of psoriasis.

The right eyes of the participants were assessed. The AS-OCT device (Cirrus HD-OCT 4000; Carl Zeiss Meditec, Inc.) was used to measure epithelial and stromal thicknesses of the conjunctiva and cornea. The anterior segment 5 line raster scanning protocol, which scans through five parallel lines all 3 mm in length and separated by 250 μ m were used to evaluate central cornea and infero-temporal bulbar conjunctiva, approximately 3 mm away from the limbus. Corneal and conjunctival images were captured and images with the least number of motion artifacts were chosen for analysis. The infero-temporal bulbar conjunctiva having minimum observational interference from the rectus muscle tendons and a lower rate of presence of conjunctival abnormalities (e.g. pinguecula) was chosen for further assessment. The epithelial and stromal thicknesses of both the conjunctiva and cornea were measured using the caliper tool on the OCT device (Figure 1). Two independent clinicians who were masked to diagnosis were carried out the OCT measurements and the values of the measurements were averaged for analysis.

SPSS software version 20.0 (SPSS Inc., Chicago,IL) was used for statistical analyses. The variables were evaluated using visual (histograms, probability plots) and analytical methods (Shapiro-Wilk test) to determine whether or not they were normally distributed. According to tests of normality, either the t test or Mann-Whitney U-test was used to compare differences between Psoriatic patients and healthy controls. Pearson or Spearman's correlation analysis was used to examine the relationship between clinical characteristics of individuals and AS-OCT measurements. The inter-examiner reproducibility of the AS-OCT measurements was assessed by measuring the intraclass correlation coefficient (ICC).

Results

We enrolled 61 eyes of 61 patients with plaque psoriasis and 42 eyes of 42 healthy controls. There were no significant differences concerning the age, gender, axial length, and intraocular pressure among the groups ($p>0.05$). (Table 1)

Table 1
Demographic and ophthalmological characteristics of psoriatic and healthy subjects.

Characteristics	Control group (mean \pm SD)	Psoriasis group (mean \pm SD)	p value
Age (years)	46.90 \pm 10.46	44.61 \pm 14.64	0.347
Gender (female/male)	24/18	34/27	0.888
Axial length (mm)	23.02 \pm 1.03	23.16 \pm 1.09	0.636
Intraocular pressure (mmHg)	15.71 \pm 3.05	15.18 \pm 3.48	0.378

The mean duration of disease was 14.29 \pm 11.33 years (range 1-50). The mean PASI score was 8.93 \pm 7.74 (range 1-35.70). Among the psoriatic patients, 37 patients (60.7%) had nail involvement; and 15 patients (24.6%) had joint involvement.

There were significant differences in terms of tear break-up time and Schirmer-1 test values between psoriasis and control groups. The results of tear functions and AS-OCT parameters were presented in Table 2. When the psoriatic patients were classified into two distinct groups, without nail psoriasis (with a mean PASI score=6.79±7.02) and with nail psoriasis groups (with a mean PASI score=10.32±7.94), the central corneal stromal thickness in patients with nail psoriasis was significantly thicker than that of controls (p<0.017).

Table 2

Clinical Test Results for Dry Eye and Ocular Surface Measurements of Patients with Psoriasis, Stratified by the Presence of Nail Psoriasis.

	Control Group (n=42)	Psoriasis Group (n=61)	Without Nail Psoriasis (n=24)	With Nail Psoriasis (n=37)	p value*	p value†
Tear break-up time test (seconds)	11.43±2.33‡	6.48±2.83	7.04±2.35‡	6.62±2.98‡	0.000	0.000
Schirmer-1 Test (mm/5 minutes)	16.00±5.89‡	12.67±6.82	12.74±6.57	12.62±7.06‡	0.007	0.025
PASI	NA	8.93±7.74	6.79±7.02	10.32±7.95	NA	0.000
Bulbar conjunctival epithelium thickness	46.18±7.06	46.45±10.07	47.19±11.17	45.97±9.43	0.716	0.883
Central corneal epithelium thickness	51.33±4.41	49.48±4.74	50.19±4.77	49.03±4.73	0.058	0.156
Bulbar conjunctival stroma thickness	191.26±63.76	169.43±43.65	179.43±40.06	162.95±45.17	0.089	0.069
Central corneal stroma thickness	454.40±52.00‡	474.57±32.61	462.07±33.17	482.68±29.96‡	0.040	0.018
*For independent samples t-test between control and psoriasis groups.						
†For Kruskal–Wallis between control, Without, and with Nail Psoriasis groups.						
‡p<0.017 (Mann-Whitney U-test with Bonferroni correction).						

PASI was positively correlated with the thickness of central cornea stroma (r=0.442, p=0.006) in nail psoriasis group. The correlations between dry eye tests and AS-OCT parameters were shown in Table 3.

Table 3
Correlations between dry eye tests and ocular surface parameters

	Control Group				Without Nail Psoriasis				With Nail Psoriasis			
	TBUT		Schirmer-1 Test		TBUT		Schirmer-1 Test		TBUT		Schirmer-1 Test	
	r	p	r	p	r	p	r	p	r	p	r	p
Bulbar conjunctival epithelium thickness	0.179	0.257	0.188	0.232	-0.313	0.136	-0.421	0.041	-0.057	0.739	0.080	0.639
Central corneal epithelium thickness	-0.114	0.471	-0.326	0.035	-0.290	0.169	0.057	0.793	0.103	0.544	-0.56	0.744
Bulbar conjunctival stroma thickness	0.012	0.939	-0.141	0.372	-0.639	0.001	-0.368	0.077	-0.072	0.674	0.091	0.591
Central corneal stroma thickness	0.047	0.766	0.160	0.310	-0.105	0.625	-0.416	0.043	-0.266	0.111	-0.356	0.031

The ICC for repeatability of AS-OCT measurements was 0.927 (95% CI: 0.852 to 0.956).

Discussion

In this cross-sectional study, significantly worse dry eye tests including tear break-up time and Schirmer-1 test values were observed in psoriasis group compared with controls. No statistically significant difference was found between psoriasis group and controls in terms of bulbar and corneal epithelial thicknesses measurements. Corneal stromal thickness values were significantly higher in psoriasis group, especially in patients with nail involvement compared with controls. Schirmer-1 test values were negatively correlated with corneal stromal thickness in psoriasis groups with and without nail involvement.

Although the psoriasis is a chronic auto-immune disease, cornea and conjunctiva structures are not extensively studied. Some strong associations between keratoconus, progressive thinning of the cornea and autoimmune diseases were found [13]. Varma et al. [14] reported peripheral corneal melting in psoriasis. The others focused on the DED related ocular surface disturbance in psoriatic patients [2–9, 15–17].

Her et al. [6] reported 36.6% of the psoriatic patients experienced dry eye. The pathogenesis of increased risk of dry eye in psoriasis is not fully understood. Similar to T-cells mediated inflammatory responses leading ocular surface epithelial metaplasia in DED [6], T-cells in psoriatic skin keratinocytes were addressed as one of the main cause of psoriasis [1]. Using conjunctival impression cytology, Karabulut et al. [4] observed higher rates of squamous metaplasia of conjunctival epithelial cells in patients with psoriasis. Furthermore, more cell alteration and decreased goblet cell density in conjunctiva were observed in psoriasis [6]. Best of our knowledge, OCT measurements of ocular surface epithelial thicknesses in psoriasis have not been reported. Moreover, the OCT studies [18–20] evaluating the ocular surface epithelial thickness have somewhat conflicting results even in dry eye. Francoz et al. [20] reported a significantly thicker bulbar conjunctival epithelium (BCE) thickness in DED and a direct relationship between ocular surface disease severity and BCE thickness but the central corneal epithelial thickness did not differ between DED and controls. Gumus et al. [19] reported no statistically significant differences in BCE and central corneal epithelial thicknesses between aqueous-deficient type DED, evaporative-type DED, and controls. Although, the BUT and Schirmer values did not correlated with both the temporal BCE and central corneal epithelial thicknesses, negative correlations between tear osmolarity and both the temporal BCE and central corneal epithelial thicknesses were observed [19]. Cui et al. [21] reported the superior corneal epithelium in DED was significantly thinner than controls. They did not observe any differences in central

corneal epithelium. The difference between central and peripheral cornea was attributed the immune and angiogenic privilege of central cornea. Liang et al. [18] reported significantly thicker bulbar conjunctival epithelium thickness in DED compared with controls but the central corneal epithelial thickness did not differ between the groups. Kanellopoulos et al. [22] reported significantly thicker central corneal epithelial thicknesses in DED compared with controls and concluded the augmented corneal epithelial thickness might be used as an objective clinical indicator of dry eye. Conversely, Ederh et al. [23] reported significant corneal epithelial thinning in DED compared with the controls. In accordance with the studies concerning DED [19–21], we observed no significant differences in BCE and central corneal epithelium thicknesses in patients with psoriasis having significantly worse dry eye test values compared with controls. The differences in epithelial thickness measurements between the studies concerning DED might be attributed to selected area differences (ie, limbal, bulber, central or peripheral), manual positioning of the caliper on selected scan to measure epithelial thickness, status of inflammation related to tear hyperosmolarity, exclusion or inclusion of the precorneal film, and precence of autoimmune diseases (eg, psoriasis). Further studies concerning cell morphology (ie, confocal microscopy) are needed to differentiate the possible causes of epithelial thickness involvement.

Using ultrasonic pachymeter [10] and OCT [11], central corneal thickness (CCT) measurements did not differ between psoriasis group and controls. Corneal biomechanical properties including corneal hysteresis (CH) and corneal resistance factor (CRF) were evaluated in psoriasis patients [10, 11]. Edris et al. [11] reported a significant negative correlation between PASI and CH and concluded that the CH might be played a role as an indicator of disease activity. In accordance with the Edris et al. [11], disease activity in the present study was negatively correlated with corneal stromal thickness and reached statistically significance in nail psoriasis group having higher PASI values. Our data supports the theory concerning the altered immune-response and T lymphocytes in psoriatic patients led subsequent weakening of corneal proteoglycans and glucosaminoglycans. However, this theory needs to be clarified with electron microscopic studies.

The involvement of corneal biomechanics in DED somewhat conflicting. Using ocular response analyzer (ORA), Firat et al. [25] reported no differences in biomechanics of the cornea. More recent studies using ORA[26] and Corneal Visualization Scheimpflug Technology (CorVis ST) [27] measurements in patients with Sjogren's disease suggested that the biomechanics of the cornea are effected in patients with Sjogren's disease.

There are some limitations of the current study. First, relatively small numbers of psoriasis patients were included. Second, we did not evaluate the serum levels of cytokins that take part in pathogenesis of psoriasis. Third limitation was only the infero-temporal conjunctiva and central cornea were evaluated. Studies with larger patient cohorts, take into account the serum levels of inflammatory cytokines, and evaluating the different parts of both conjunctiva and cornea are now required to detect the ocular surface involvement more precisely.

In conclusion, Psoriasis is associated with the DED. This is the first report of epithelial and the stromal thickness changes of both the conjunctiva and cornea in psoriasis. Further studies are needed to clarify the causes of central corneal stromal thickening in psoriasis.

Declarations

Author contribution All authors contributed to the study conception and design. IE, SK, and SI contributed to the acquisition of data. IE and SK contributed to the analysis and interpretation of data. IE, SK, and SI drafted the manuscript. IE, SK, and SI were involved in critical revision. All authors read and approved the final manuscript.

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Data availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no proprietary or financial interest in any product mentioned in this article.

Ethical approval This study was approved by the Clinical Research Ethics Committee of Canakkale Onsekiz Mart University School of Medicine and followed the tenets of the 1964 Declaration of Helsinki.

Informed consent Informed consent was taken before each individual's participation in this study

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Figures

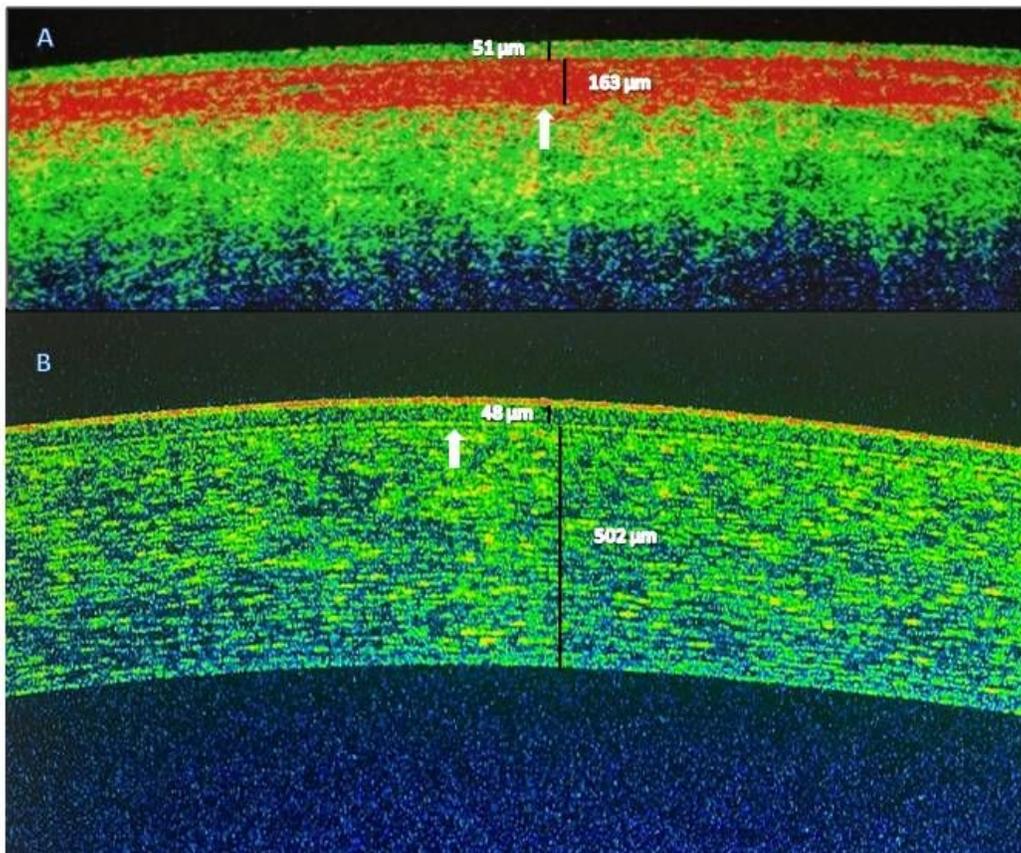


Figure 1

Anterior segment optical coherence tomography images of a patient in control group. (A) Epithelial and stromal conjunctival thicknesses of infero-temporal bulbar conjunctiva, approximately 3.0 mm away from the limbus. Below the high reflective layer (conjunctival stroma), there was a progressively lower reflective layer (Tenon's capsule) with a narrow demarcation (white arrow). (B) Epithelial and stromal corneal thicknesses of central cornea. Below the corneal epithelium, there was the basal epithelial membrane separated from the underlying corneal stroma.