

Corneal Thickness in Patients with Age-related Macular Degeneration

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This observational study was designed to compare corneal thickness in patients with age-related macular degeneration (AMD) with the thickness in healthy control subjects to determine if there is a correlation between corneal thickness and the development of AMD. A total of 69 patients (119 eyes) with AMD and 31 healthy subjects (56 eyes) were evaluated. Corneal thickness was measured with a Galilei™ Dual Scheimpflug Analyser and

retinal thickness was measured using optical coherence tomography. There was no significant difference in mean corneal thickness or mean retinal thickness between the AMD and control groups and no correlation between corneal and retinal thickness in either group. The results confirmed that corneal thickness is not associated with the development of AMD and cannot be used during diagnosis.

KEY WORDS: AGE-RELATED MACULAR DEGENERATION (AMD); CORNEAL THICKNESS; GALILEI™ DUAL SCHEIMPFLUG ANALYSER; RETINAL THICKNESS; OPTICAL COHERENCE TOMOGRAPHY; RISK FACTOR

Introduction

Age-related macular degeneration (AMD) is defined as a progressive degeneration of the macula lutea in elderly patients. It is the most prominent cause of permanent loss of vision in the developed world among people > 60 years of age, it affects over 25 million people worldwide and it has a profound impact on vision-related quality of life.¹⁻³ The disease affects both genders equally and occurs more frequently in Caucasians.⁴⁻⁸ AMD is a complex disease of unknown aetiology, but there is thought to be a strong genetic component in its pathogenesis, with genetic defects found in 75% of AMD patients.^{5,9} In addition to the genetic component, there are several known environmental factors associated with its

occurrence, such as smoking, obesity, hypertension, atherosclerosis, diet and cataract surgery.¹⁰⁻¹³ Corneal thickness is associated with systemic ocular conditions like active Behçet's disease, Down's syndrome, diabetes mellitus, osteogenesis imperfecta, keratoconus, dry eye, glaucoma and retinal detachment,^{7,8,14-23} and the changes in corneal thickness are clinically very important.²⁴

Corneal thickness is usually measured using ultrasound pachymetry. This technique has several negative features, such as the need to use local anaesthetics, direct contact between the device and the cornea resulting in an increased risk of infection, inappropriate positioning of the device, and different speeds of sound in variously

hydrated tissues.^{25,26} Recently, newer devices, based on a rotating dual Scheimpflug camera, have been introduced for use in this area of ophthalmology; e.g. the Galilei™ and Pentacam corneal topography systems.^{27,28} Galilei™ is a non-invasive diagnostic system designed for analysis of the anterior chamber of the eye in which a rotating dual Scheimpflug camera is integrated with a Placido topographer. It measures corneal thickness by pachymetry. Non-contact instruments have the advantage of being able to create a pachymetry map of thickness readings across the cornea as opposed to the set of single readings provided by ultrasound pachymetry.^{29,30} In addition, with the development of optical coherence tomography (OCT), new possibilities for retinal diagnosis have become possible.³¹⁻³⁵

This study was designed to compare corneal thickness between patients with AMD and a group of healthy subjects using a Galilei™ Dual Scheimpflug Analyser to determine whether there is a correlation between corneal thickness and the development of AMD.

Patients and methods

PATIENT POPULATION

This observational study included patients with AMD who were treated at the Department of Ophthalmology, University Clinical Centre Maribor, Slovenia, between April and August 2008, and a group of control subjects who were recruited from healthy individuals admitted to the Department of Ophthalmology for preventive ophthalmic examination. Participants in both groups were > 60 years old with no known corneal pathology. The study excluded all patients with AMD who had other ocular conditions that might have influenced corneal thickness (e.g. previous

eye surgery, corneal pathology, previous corneal disease, ocular trauma, contact lens users, tear film pathology and diabetes mellitus). Since this was a routine observational study there was no need for ethics committee approval. All of the participants were acquainted with the procedure and purpose of the study. After verbal informed consent was obtained, a complete medical history and examination were undertaken. The medical history included whether there was current or previous ocular disease or trauma, general health status and therapies used. The date of AMD diagnosis and the last noted deterioration in visual acuity were also recorded.

OPHTHALMIC EXAMINATIONS

All participants underwent a complete ophthalmic examination including visual acuity, slit-lamp biomicroscopy and stereoscopic fundus evaluation in mydriasis.

Corneal thickness was measured at four different locations: at the central, paracentral and peripheral zones, and at the thinnest point. The anterior chamber depth and pupil diameter were also measured in all participants. All measurements were made with a Galilei™ Dual Scheimpflug Analyser, version 3.0 (Ziemer Ophthalmic Systems AG, Port, Switzerland).

Mean retinal thickness was evaluated with OCT using the Zeiss Stratus OCT system, version 4.0.1 (Carl Zeiss Meditech Ophthalmic Systems Inc., Dublin, CA, USA), which is based on the principle of Michelson interferometry.³⁶⁻³⁸ Light passing through the eye is reflected by structures in different retinal tissue layers. Moving the light source over the retinal surface produces a two-dimensional, cross-sectional image that resembles a histology section. The instrument electronically detects, collects,

processes and stores the echo delay patterns from the retina. It displays the tomograms in real-time using a false colour scale that represents the degree of light backscattering from tissues at different depths in the retina.

STATISTICAL ANALYSIS

Data were evaluated using descriptive analyses. Student's *t*-test and Pearson's correlation test were applied. Data were analysed using the SPSS® statistical package, version 15.0 (SPSS Inc., Chicago, IL, USA) for Windows®. A *P*-value of < 0.05 was considered to be statistically significant.

Results

This study evaluated 69 patients (119 eyes) with AMD (51 women, 18 men) and a control group of 31 healthy subjects (56 eyes) (20 women, 11 men). The mean \pm SD age in the AMD group was 74.3 ± 7.9 years (range 60 – 89 years) and in the control group was 73.0 ± 7.0 years (range 61 – 86 years). There was no significant difference in mean age between the two groups. The two groups were also comparable for gender distribution: 73.9% women in the AMD group versus 64.5% women in the control group.

There were no statistically significant differences between the AMD group and the control group in the mean \pm SD corneal thickness in the central, paracentral and peripheral zones or at the thinnest point of the cornea (Table 1; Figs 1 – 4). There was, however, a difference between the two groups in the minimum and maximum corneal thickness for all locations, with the exception of the maximum values for the central zone and thinnest point.

Mean retinal thickness was evaluated in 68 patient AMD patients (117 eyes) and 29 healthy subjects (53 eyes) (Table 2). Due to cataracts, it was not possible to measure

retinal thickness in two eyes (one patient) in the AMD group and three eyes (two patients) in the control group. There was no statistically significant difference in mean \pm SD retinal thickness between the AMD and the control groups (Table 2; Fig. 5), although there was a difference between the two groups in the minimum and maximum retinal thicknesses.

The anterior chamber in the control subjects was significantly deeper than in the AMD patients ($P = 0.002$) (Table 3). There were no significant differences in pupil diameter or intra-ocular pressure between the two groups.

Pearson's correlation test showed no statistically important linear correlation between corneal and retinal thickness in the AMD ($r = 0.067$) and control groups ($r = 0.074$).

Discussion

The aetiology of AMD is still unknown but it is related to many known risk factors. AMD is a disease of epidemic proportions, so it is very important to accelerate the development of medicines and the quality of healthcare in the various European countries.³⁹ A reduced corneal thickness was expected among AMD patients in the present study, as this is thought to be an additional risk factor for AMD development. This expectation was based on the hypothesis that oxidative damage to the retinal pigment epithelium is influenced by exposure to sunlight and on the protective role played by a healthy cornea, which is the most important refractory medium in the human eye. According to this hypothesis, sunlight damages the cornea (this could be evident from corneal thickness) and, therefore, enters the eye to affect the retina. Thus, the present study investigated whether a direct correlation existed between corneal thickness and AMD. Contrary to

TABLE 1:
Comparison of corneal thickness measured by pachymetry at four locations in 69 patients (119 eyes) with age-related macular degeneration (AMD) and 31 healthy control subjects (56 eyes) using a Galilei™ Dual Scheimpflug Analyser

Location	Group	No. of eyes, n	Corneal thickness (µm)			Statistical significance
			Mean ± SD	Minimum	Maximum	
Central zone	AMD (n = 69)	119	569.66 ± 36.89	393	654	NS
	Control (n = 31)	56	567.00 ± 35.92	501	674	
Paracentral zone	AMD (n = 69)	119	606.56 ± 43.48	402	685	NS
	Control (n = 31)	56	607.57 ± 63.45	528	980	
Peripheral zone	AMD (n = 69)	119	653.56 ± 65.70	297	742	NS
	Control (n = 31)	56	646.11 ± 61.01	503	950	
Thinnest point	AMD (n = 69)	119	534.02 ± 73.27	229	642	NS
	Control (n = 31)	56	519.07 ± 89.68	86	626	

NS, not statistically significant ($P > 0.05$).

TABLE 2:
Comparison of retinal thickness in 68 patients (117 eyes) with age-related macular degeneration (AMD) and 29 healthy control subjects (53 eyes) measured using a Zeiss Stratus optical coherence tomography system

Group	No. of eyes, n	Retinal thickness (µm)			Statistical significance
		Mean ± SD	Minimum	Maximum	
AMD (n = 68) ^a	117	220.03 ± 46.56	80	507	NS
Control (n = 29) ^a	53	209.60 ± 21.93	167	285	

^aDue to cataracts, it was not possible to measure retinal thickness in two eyes (one patient) in the AMD group and three eyes (two patients) in the control group.

NS, not statistically significant ($P > 0.05$).

Corneal thickness is unrelated to AMD

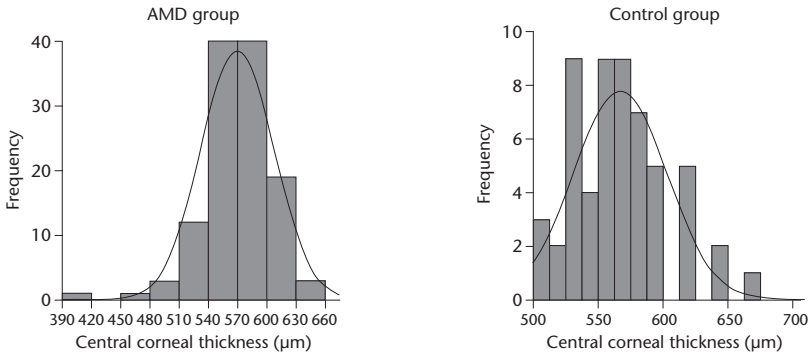


FIGURE 1: Distribution of central corneal thickness amongst 69 patients (119 eyes) with age-related macular degeneration (AMD) and 31 healthy control subjects (56 eyes) measured using a Galilei™ Dual Scheimpflug Analyser

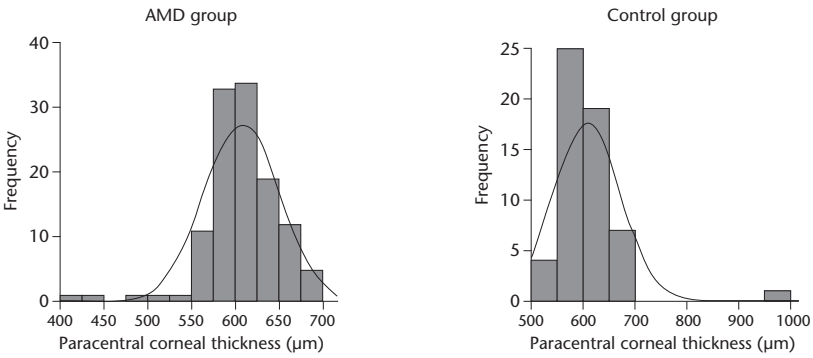


FIGURE 2: Distribution of paracentral corneal thickness amongst 69 patients (119 eyes) with age-related macular degeneration (AMD) and 31 healthy control subjects (56 eyes) measured using a Galilei™ Dual Scheimpflug Analyser

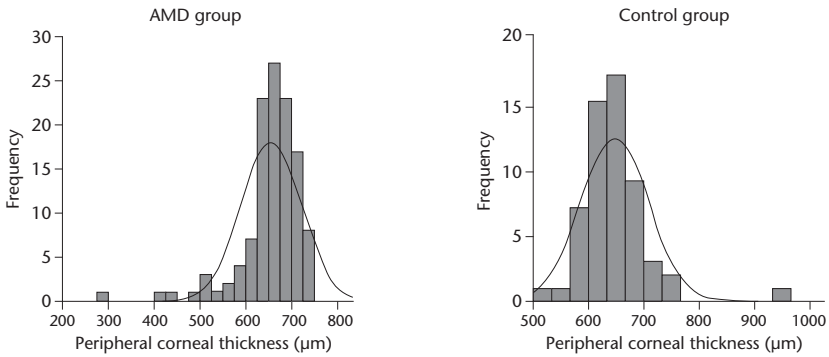


FIGURE 3: Distribution of peripheral corneal thickness amongst 69 patients (119 eyes) with age-related macular degeneration (AMD) and 31 healthy control subjects (56 eyes) measured using a Galilei™ Dual Scheimpflug Analyser

Corneal thickness is unrelated to AMD

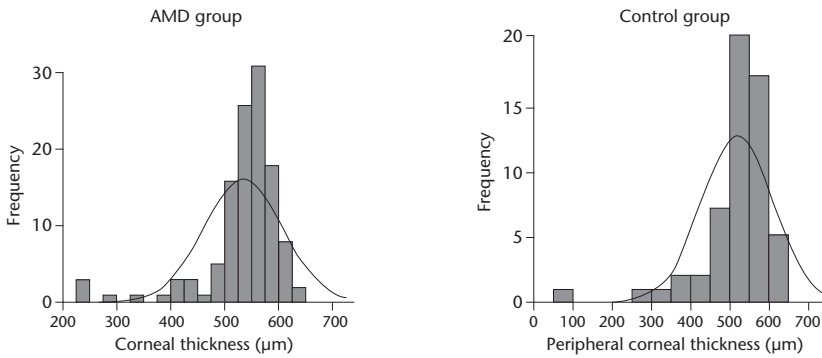


FIGURE 4: Distribution of the thickness (μm) of the thinnest point of the cornea amongst 69 patients (119 eyes) with age-related macular degeneration (AMD) and 31 healthy control subjects (56 eyes) measured using a Galilei™ Dual Scheimpflug Analyser

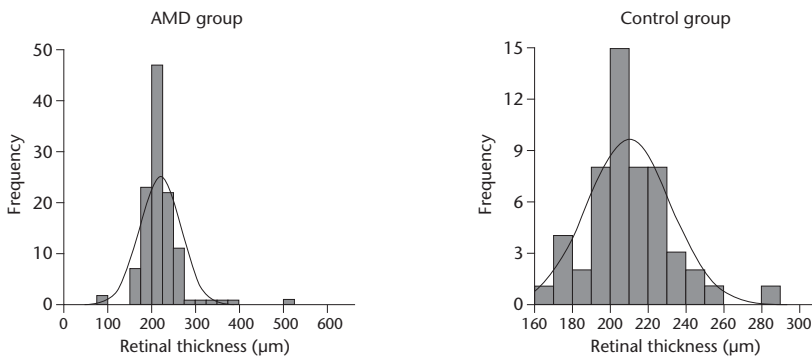


FIGURE 5: Distribution of retinal thickness amongst 68 patients (117 eyes) with age-related macular degeneration (AMD) and 29 healthy control subjects (53 eyes) measured using a Zeiss Stratus optical coherence tomography system

expectations, after completing the ocular examination and the described diagnostic procedures, it was concluded that there was no statistically significant difference in mean corneal thickness in any of the four measured zones between the AMD patients and the control group.

These findings are very important in the search for additional risk factors for AMD. They showed that measuring corneal thickness during the AMD diagnostic examination is irrelevant. Similar results were obtained from a previous study that

measured central corneal thickness, albeit using a different diagnostic device, ultrasound contact pachymetry.⁴⁰ Despite the fact that the present study included a different number of participants, neither study demonstrated a significant difference in corneal thickness between AMD patients and control subjects. The earlier study implied that the measurements of corneal thickness obtained using ultrasound contact pachymetry were not as accurate as those obtained using the newer device that was used in the present study.⁴⁰

TABLE 3: Comparison of anterior chamber depth, pupil diameter and intra-ocular pressure in 69 patients (119 eyes) with age-related macular degeneration (AMD) and 31 healthy control subjects (56 eyes)

Location	Group	No. of eyes, n	Mean \pm SD	Minimum	Maximum	Statistical significance
Anterior chamber depth (mm)	AMD (n = 69)	119	2.44 \pm 0.34	1.49	3.37	P = 0.002
	Control (n = 31)	56	2.61 \pm 0.34	1.88	3.31	
Pupil diameter (mm)	AMD (n = 69)	119	2.68 \pm 1.30	0.49	8.00	NS
	Control (n = 31)	56	2.80 \pm 1.34	0.18	7.16	
Intra-ocular pressure (mmHg)	AMD (n = 69)	119	16.56 \pm 2.66	10	24	NS
	Control (n = 31)	56	16.04 \pm 2.64	10	21	

NS, not statistically significant ($P > 0.05$).

Previously, considerable research efforts have been focused on finding the risk factors for AMD, including the influence of sunlight.^{9,41,42} From a clinical point of view, these findings suggest that sunlight somehow contributes to the appearance of AMD. Based on data acquired in the present study, however, it could be concluded that the amount of daily sunlight exposure does not cause corneal impairment that could contribute to the occurrence of AMD, and that corneal thinning is not the means by which sunlight exerts its influence. Additionally, retinal thickness measurements showed no statistically significant difference between the AMD and control groups although, as expected, mean retinal thickness was slightly higher in AMD patients. Pearson's correlation test found no correlation between the corneal and retinal thicknesses in either group.

The only statistically significant difference between the two groups was the mean anterior chamber depth, which was significantly deeper in the control group. Whether or not the anterior chamber depth is important in the occurrence of AMD is a matter for further investigation. Lens thickness could also be a possible risk factor for the development of AMD, but neither anterior chamber depth nor lens thickness have been fully investigated as potential risk factors for AMD.

The results from the two groups in the present study were comparable and, even though the number of examined eyes was different between the two groups, they did not differ in terms of the parameters that could interfere with corneal thickness. Although it is not currently possible to predict which patients might develop AMD in the future, further investigations could measure corneal thickness over a longer period of time, starting from before the onset of AMD and continuing throughout the

course of the disease. Future studies could also compare corneal thickness in AMD patients in different age groups and at different stages of disease.

In conclusion, this is the first study in which the latest non-contact method of corneal pachymetry has been used to evaluate corneal thickness as a possible pathophysiological mechanism in the pathogenesis of AMD. The results confirmed

that corneal thickness is not associated with the development of AMD. Further investigations are necessary to confirm these findings and to determine whether anterior chamber depth may be a possible additional risk factor for AMD development.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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