Measurement of Subfoveal Choroidal Thickness Using Spectral Domain Optical Coherence Tomography

Emily A. McCourt, MD; Brian C. Cadena, PhD; Cullen J. Barnett, CRA; Antonio P. Ciardella; Naresh Mandava, MD; Malik Y. Kahook, MD

■ BACKGROUND AND OBJECTIVE: To compare subfoveal choroidal thickness (SFCT) in normal patients and those with known ocular pathology using spectral domain optical coherence tomography (SD-OCT).

■ PATIENTS AND METHODS: This retrospective, observational case series was conducted at a tertiary care center where 194 consecutive eyes from 102 patients were imaged. Patients were not included or excluded based on presence or absence of pathology. One masked observer imaged the choroid and a second masked observer measured SFCT. Multivariate analysis was used and a statistical model created to analyze the changes in SFCT induced by age, diabetic retinopathy, glaucoma, wet and dry age-related macular degeneration, and other posterior pole pathology.

■ RESULTS: The mean SFCT of the 194 eyes studied was 246.59 ± 93.17 µm with a mean age of 55.50 ± 19.70 years. A strong negative relationship was found between age and SFCT ($R^2 = 0.42$), with an average 3.09-µm decrease in SFCT per additional year of age. Subgroup analysis demonstrated that patients with diabetic retinopathy, wet or dry age-related macular degeneration, and glaucoma all had SFCT measurements that were statistically significantly less than those of normal patients. However, when regression analysis was used to control for age, this difference was no longer significant.

■ CONCLUSION: No differences were found in SFCT in patients with glaucoma, macular degeneration, or diabetic retinopathy compared to eyes lacking pathology when age was counted as a confounding variable. Age has a strong inverse relationship with SFCT, independently confirming prior studies and creating a foundation for more research on the relationship between ocular pathology and choroidal thickness.

[Ophthalmic Surg Lasers Imaging 2010;41:S28-S33.]
INTRODUCTION

The choroid serves many essential functions for the eye. It acts as a heat sink for the retina\textsuperscript{1,2} and delivers blood to 85% of the eye, including the photoreceptors and the prelaminar portion of the optic nerve head.\textsuperscript{3} Despite its importance, we have few reliable techniques to study choroidal structure and function.\textsuperscript{4} Disturbance of choroidal blood flow may play a key role in disease states such as glaucoma, diabetic retinopathy, and age-related macular degeneration (AMD).\textsuperscript{3,5,6} Resistance to flow is related to the diameter of a vessel\textsuperscript{3}; thus, choroidal thickness may be proportional to the blood flow in the choroid and may be an important metric for choroidal health. Therefore, it is important to study choroidal thickness with more precision to better understand this vital structure.

A novel way for measuring the thickness of the choroid was recently described in patients without any underlying pathology.\textsuperscript{7} A decrease in subfoveal choroidal thickness with increasing age was also recently reported.\textsuperscript{1} Subfoveal choroidal thickness in patients with AMD, diabetic retinopathy, and glaucoma has not been reported in peer-reviewed literature to our knowledge. We report the results of our retrospective review that details the ability of spectral domain optical coherence tomography (SD-OCT) to measure subfoveal choroidal thickness in a tertiary care center in both normal patients and patients with various ophthalmic diseases.

PATIENTS AND METHODS

This is a retrospective consecutive case series of patients who underwent subfoveal choroidal thickness measurements at the Department of Ophthalmology at the University of Colorado Denver between January and June 2009. One hundred ninety-four eyes of 102 consecutive patients were scanned using the Heidelberg Spectralis SD-OCT machine (Heidelberg Engineering, Heidelberg, Germany). The study included eyes with a variety of pathology and patients were not excluded or included in the study based on any known eye disease or lack thereof. The eyes classified as normal controls did not have any pathology other than mild to moderate cataracts.

The choroid was imaged using the same method as previously described\textsuperscript{7} by positioning the SD-OCT device closer to the eye to create an inverted image (Figs. 1A and 1B). The image color was changed from black on white to white on black to increase the contrast between the choroid and the sclera to measure the choroidal thickness more accurately (Fig. 1C). The subfoveal choroidal thickness was measured by a masked observer using the calipers within the software of the OCT machine and positioning them from the outer aspect of Bruch’s membrane to the border of the sclera.

The data were analyzed using STATA software (StataCorp, College Station, TX). Each eye was treated as a separate observation in all analyses. Standard errors from the regression analysis were adjusted for potential within-patient correlation. The resulting standard errors provide valid statistical inference even if choroidal thickness is more similar in two eyes from the same patient than in two randomly sampled eyes. This was done to prevent doubling our data because, for example, diabetic retinopathy tends to be a bilateral disease process.
RESULTS

Tables 1 and 2 provide an overview of our patient population. The overall mean subfoveal choroidal thickness was 246.59 ± 93.2 µm and the overall mean age was 55.5 ± 19.7 years. Figure 2 shows a histogram of subfoveal choroidal thickness in our patient population.

Mean subfoveal choroidal thickness was 198.3 µm for eyes with glaucoma (n = 18) and 221.7 µm for eyes with diabetic retinopathy (n = 30). Average subfoveal choroidal thickness was 209.9 µm for eyes with wet AMD (n = 15) and 162.4 µm for eyes with dry AMD (n = 15). The 39 eyes with posterior pole pathology that did not fit into one of the above categories had a mean subfoveal choroidal thickness of 252.3 µm. Normal eyes (n = 63) had a mean subfoveal choroidal thickness of 305.7 µm. As demonstrated in Table 3, when compared to the normal groups, all pathologies evaluated had a statistically significant decrease in subfoveal choroidal thickness. However, when regression analysis was used to control for patient age, none of the differences in subfoveal choroidal thickness remained statistically significant (Table 4).

With regression analysis, several models for choroidal thickness as a function of age and adjustment for pathology were fitted (Table 4). The simplest regression model includes only age as an explanatory variable, and the results suggest that choroidal thickness falls by approximately 3.085 µm per year. The R² value demonstrates the strength of the relationship of subfoveal choroidal thickness to age. In our study, age accounted for 42% of the variation in subfoveal choroidal thickness. Figure 3 plots patient age and subfoveal choroidal thickness for the entire sample and the fitted line from the regression model using only age as a covariate. The same analysis with normal eyes can be seen in Figure 4. In addition, Figure 5 displays each point according to the presence and type of pathology.

The remaining question is whether eyes with pathology deviate from their age-adjusted expected thicknesses in any systematic way. The figure does not provide any obvious support for that hypothesis, and the regression results confirm that we cannot reject the null hypothesis that eyes with varying pathologies and normal eyes have equal subfoveal choroidal thickness after accounting for age. In this model, glaucoma would add approximately 5.6 µm to a patient’s age-adjusted subfoveal choroidal thickness and diabetes mellitus would add 8.89 µm. Wet AMD would add 47.78 µm and dry AMD would subtract 14.1 µm. However, none of these differences are statistically significantly different from zero.
DISCUSSION

This study details the measurement of subfoveal choroidal thickness in a variety of ophthalmic diseases and compares these findings to eyes lacking pathology. The major contribution of this study is the finding of a strong inverse relationship between subfoveal choroidal thickness and age. This finding independently confirms and further extends the work done by Spaide et al. and provides information to build on for future prospective studies.\(^1,2\)

Patients with diabetic retinopathy were found to have increased subfoveal choroidal thickness compared with the overall study population, but this difference was not statistically significant when accounting for differences in age. This finding was somewhat surpresa-
correlate choroidal blood flow to subfoveal choroidal thickness. The prospect for such studies is currently limited by the lack of precise tools for measuring blood flow in choroidal vessels.

The choroidal thickness in eyes with dry AMD was 14.07 µm thinner than was expected when controlled for age. However, this result was not statistically significant due to the high standard error. This is probably best explained by the very strong relationship that both AMD and choroidal thickness have with age. Thus, a higher powered study may prove AMD and age to be additive in the future. Eyes with wet AMD were found to have a subfoveal choroidal thickness that was 47.78 µm thicker than expected for adjusted age. This result was also not statistically significant due to high standard error. This was an unexpected result because multiple previous studies have shown choroidal thickness and blood flow to be decreased in patients with wet AMD. Additionally, both choroidal thickness and choroidal blood flow have been proven to be decreased in patients with wet AMD compared with those with dry AMD.\(^5\) A possible explanation for this finding is the increased vasculature and vascular endothelial growth factor release that is associated with wet AMD.\(^8\)

It is noteworthy that decreased choroidal blood flow and volume as measured by Doppler laser has been demonstrated in patients with AMD\(^4\) and has been shown prospectively to indicate higher risk of disease progression.\(^5\) Metelista et al. found a thinner choroid in patients with the wet variety of AMD,\(^5\) which is the opposite of what we found in our patients. Again, due to the extremely strong relationship between both subfoveal choroidal thickness and AMD with age, we
would need a larger number of patients to achieve the power required to demonstrate a statistically significant difference and further studies are underway to explore these relationships.

The average subfoveal choroidal thickness in patients with glaucoma in our study was 5.59 µm thicker than would have been expected when controlled for age. However, this result was not statistically significant. Decreased ocular blood flow in glaucoma has been reported, although a direct causal relationship has not been firmly established. The disruption of oxygenated blood flow to the retina and optic nerve head might lead to ischemia and cell apoptosis with eventual loss of ganglion cells and thinning of the optic nerve head rim. Still, it is unclear how this would relate to the fact that the choroid serves 85% of the outer retina, and most of these structures are spared while the inner portion of the retina (the ganglion cells) is injured. Additionally, our study did not find any difference in subfoveal choroidal thickness when the data were controlled for age.

There are important limitations in this study. This was a retrospective study of a limited number of consecutive patients. The group of patients used was heterogeneous with a variety of ophthalmic pathology and a wide range of ages. Additionally, we did not account for the sub-population differences such as the type of glaucoma or diabetic retinopathy. Another limitation was the younger age and smaller number of normal patients used as controls in this study. Because most of our pathology was found in patients with advanced ages, and the negative relationship between subfoveal choroidal thickness and age is so strong (R² = 0.42), we will need a more highly powered study to tease out differences if they exist.

There are no related studies that we can use to compare our data because our study is, to the best of our knowledge, the first to compare the subfoveal choroidal thickness of different pathologies using the Spectralis OCT. We did find a much greater decrease in subfoveal choroidal thickness with age in normal eyes when compared with previous data published by Spaide et al., who found a 1.56-µm decrease in subfoveal choroidal thickness with each year. The difference between our results can be explained by the different populations studied. We had a larger population of normal patients who were younger than those previously studied. This could cause the steeper slope in our regression line. Additionally, we measured the subfoveal choroidal thickness from the outer border of Bruch’s membrane, whereas Spaide et al. used the outer border of the retinal pigment epithelium as their landmark. This would make our measurements thinner and would not explain the increase in subfoveal choroidal thickness that we found in our patient population when compared with previously reported data.

Future prospective studies of patients with glaucoma, AMD, and diabetic retinopathy will help us to better understand the role that the choroid plays in the pathophysiology of these diseases and perhaps help us better predict morbidity in these patients. In addition, although the subfoveal choroidal thickness does reflect the anatomic thickness of the choroid, further studies will be needed to establish a correlation between subfoveal choroidal thickness and the volume or rate of choroidal blood flow. Measurement of subfoveal choroidal thickness is a noninvasive method to image the choroid and may prove to be a reliable metric to diagnose disease, monitor response to therapy, or monitor progression of disease. Further studies are needed to understand the full potential of this mode of imaging.

REFERENCES