• Comment and Response •

Comment on "The thickness and volume of the choroid, outer retinal layers and retinal pigment epithelium layer changes in patients with diabetic retinopathy"

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Received: 2019-02-27 Accepted: 2019-03-19

DOI:10.18240/ijo.2019.08.23

Citation: Călugăru D, Călugăru M. Comment on "The thickness and volume of the choroid, outer retinal layers and retinal pigment epithelium layer changes in patients with diabetic retinopathy" *Int J Ophthalmol* 2019;12(8):1366-1368

Dear Editor,

We would like to address several issues that have arisen from the study by Wang *et al*[1]. The study was retrospectively conducted and evaluated the thickness and volume changes of the choroid, outer retinal layers (ORL), and retinal pigment epithelium (RPE) in patients with diabetic retinopathy (DR) using optical coherence tomography (OCT) and correlated them with visual acuity.

The authors defined the ORL thickness as the layers from the RPE to the external limiting membrane (ELM), that is, the sum of the length of the inner and outer segments of the photoreceptors. We wonder why the outer nuclear layer (ONL), which is a part of the photoreceptor cell layer, was not included in this definition. Moreover, the thickness of the inner retinal layers, whose data are given in the Table 2, was not clearly defined as the authors did with the definition of the RPE thickness. Taken together these issues make interpretation of the results challenging.

There were significant differences between the non-diabetic macular edema (DME) and DME groups with respect to the best-corrected visual acuity (BCVA) score (75 and 65 Early Treatment Diabetic Retinopathy Study letters, respectively) and the level of the Hemoglobin A1c (7.3 and 9.1%, respectively). These findings certify a definite difference in the evolution stage of the diabetes between the two groups. Accordingly, patients in the non-DME group had a significantly less-progressed disease compared with those in the DME group. There were no details with regard to the type (1/2) of diabetes, the stages of DR (mild, moderate, and severe nonproliferative and proliferative DR), and the DME, which is most commonly classified into being clinically significant or not and center-involved/non-center-involved. Nothing was stated with respect to the stratification of the DME eyes by OCT patterns (sponge-like swelling/cystoid macular edema/subfoveal neuroretinal detachment/mixed type) as well as the location of the cystoid type (ganglion cell layer,/inner/outer nuclear layers) if it existed in some cases[2-3] of the DME group.

There were no data referring to the damages of the photoreceptor cell layers comprising thinning of the ONL, ELM band defects allowing fluid to enter the retina and causing “cystoid macular degeneration”, ellipsoid zone disruption, interdigitation zone loss, and hyperreflective foci in the neuroretina and subretinal space. These changes could have been better correlated with BCVA score than did the assessment of the thickness of the choroid, ORL, and RPE. Likewise, the evaluation of the alterations in the various segments of the inner retinal layers, that is, the ganglion cell complex, inner nuclear layer, and outer plexiform layer could have been better linked with the BCVA score than did the overall assessment of the thickness of the inner retinal layers. The same thing can be said about the evaluation of the changes of the retinal pigment epithelial band-Bruch membrane complex [pigment migration within the neurosensory retina, retinal pigment epithelium (RPE) porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE thickening, presence of reticular pseudodrusen, and diffuse ooze within or adjacent to the decompensated RPE] compared with the overall assessment of the RPE thickness[4].

Nothing was stated concerning the existence or otherwise of a diabetic choroidopathy, which consists in intrachoroidal vascular abnormalities and which may directly induce choroidal ischemia, leading to RPE dysfunction. The authors of this study ascertained that the mean choroidal thickness in both the non-DME and DME groups was decreased significantly compared with the control group. On the contrary, Kim *et al*[5] documented progressive thickening of the choroid layer caused by increasing the severity of DR (from no DR to proliferative DR) and development of DME (being thickest in eyes with

serous neuroretinal detachment type of DME), which denotes the progression of diabetic choroidopathy.

Altogether, the authors of this series concluded that the choroid, ORL, and RPE thicknesses are significantly decreased in DR patients compared with controls in different segments. However, nothing was stated regarding the significance of the significant increase in the thickness of the inner retinal layers in patients of the DME group as well as the need to assess this change in all segments of the inner retinal layers.

ACKNOWLEDGEMENTS

All authors were involved in design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript.

Conflicts of Interest: Călugăru D, None; **Călugăru M,** None.

REFERENCES

1 Wang XN, Li ST, Li W, Hua YJ, Wu Q. The thickness and volume of the choroid, outer retinal layers and retinal pigment epithelium layer changes in patients with diabetic retinopathy. *Int J Ophthalmol* 2018;11(12): 1957-1962.

2 Călugăru D, Călugăru M. Choroidal thickness changes stratified by outcome in real-world treatment of diabetic macular edema. *Graefes Arch Clin Exp Ophthalmol* 2019;257(1):241-242.

3 Călugăru D, Călugăru M. Anti-VEGF treatment for diabetic macular edema in a real-world clinical setting. *Am J Ophthalmol* 2018;196:208-209.

4 Călugăru D, Călugăru M. Guidelines on diabetic eye care. The International Council of Ophthalmology. Recommendations for screening, follow-up, referral, and treatment based on resources settings. *International Journal of Development Research* 2018;8(9): 22645-22646.

5 Kim JT, Lee DH, Joe SG, Kim JG, Yoon YH. Changes in choroidal thickness in relation to the severity of retinopathy and macular edema in type 2 diabetic patients. *Invest Ophthalmol Vis Sci* 2013;54(5):3378-3384.

Author Reply to the Editor

Dear Editor,

We very much appreciate Professor Dan Călugăru and Mihai Călugăru's comments on our study of the thickness and volume of the choroid, outer retinal layers and retinal pigment epithelium (RPE) layer changes in patients with diabetic retinopathy (DR).

In our study, segmentation of the retinal layers was performed on a horizontal macular volume scan using new auto-segmentation software (version 6.3.1.0; Segmentation Technology; Heidelberg Engineering, Inc.). The definitions of the outer/inner retinal layers were clearly described in our other article[1]. In another study, conducted by Nakamura[2], outer retinal layer thickness was also defined as the distance between the outer border of the external limiting membrane and the inner border of the retinal pigment epithelium. Therefore, different classification methods for retinal structures may be due to different versions of software or different patterns of OCT.

Many previous studies have shown that the stratification of the DME eyes by OCT patterns (sponge-like swelling/cystoid macular edema/subfoveal neuroretinal detachment/mixed type) as well as the location of the cystoid type (ganglion cell layer/inner/outer nuclear layers) can affect the structure and function of the retina[3-4]. We had not conducted further research in more detail. In our previous study, we had evaluated variations in choroidal thickness in different patterns of DME, as demonstrated by fluorescein angiography and optical coherence tomography (OCT)[4].

Also, ELM band defects, ellipsoid zone disruption, interdigitation zone loss, and hyperreflective foci in the neuroretina and subretinal space have been confirmed correlated with BCVA[5]. Likewise, it had been said that the evaluation of the changes of the retinal pigment epithelial band-Bruch membrane complex, the ganglion cell complex, inner nuclear layer, and outer plexiform layer could have been better linked with the BCVA[6]. However, the topic of study is to study the thickness and volume of the choroid, outer retinal layers and retinal pigment epithelium layer changes in patients with diabetic retinopathy. The study of more detail factors can make our conclusions more convincing, which is also the direction of our further research.

Kim *et al*[7] had documented choroidal thickness increased significantly as the severity worsened from mild/moderate/no proliferative DR to proliferative DR. However, in their study mean subfoveal choroidal thickness (SFChT) in groups with no DR (40 eyes), was 262.3±68.4 μm was thicker than mild/moderate no proliferative DR 244.6±77.0 μm. In our study, we did not incorporate the patients with proliferative DR into research. Also, as we had mentioned in the limitation, the small sample size and selection bias of the study would cause discrepancy in our results. SFChT had been reported they were significantly reduced in patients with proliferative DR and DME[8]. There are many other factors (gender, age, eye axis) that affected the choroidal thickness[9-10]. With the development of analysis techniques and software, further studies should be performed to elucidate choroidal thickness changes in DME. Thanks again for the evaluation of our research and looking forward to more exchanges and cooperation.

REFERENCES

1 Li ST, Wang XN, Du XH, Wu Q. Comparison of spectral-domain optical coherence tomography for intra-retinal layers thickness measurements between healthy and diabetic eyes among Chinese adults. *PLoS One* 2017;12(5):e0177515.

2 Nakamura T, Ueda-Consolvo T, Oiwake T, Hayashi A. Correlation between outer retinal layer thickness and cone density in patients with resolved central serous chorioretinopathy. *Graefes Arch Clin Exp*

Ophthalmol 2016;254(12):2347-2354.

3 Kang SW, Park CY, Ham DI. The correlation between fluorescein angiographic and optical coherence tomographic features in clinically significant diabetic macular edema. *Am J Ophthalmol* 2004;137(2):313-322.

4 Wang X, Li S, Li W, Hua Y, Wu Q. Choroidal variations in diabetic macular edema: fluorescein angiography and optical coherence tomography. *Curr Eye Res* 2018;43(1):102-108.

5 Lee JH, Kim JY, Jung BJ, Lee WK. Focal disruptions in ellipsoid zone and interdigitation zone on spectral-domain optical coherence tomography in pachychoroid pigment epitheliopathy. *Retina* 2018.

6 Chen Y, Li J, Yan Y, Shen X. Diabetic macular morphology changes may occur in the early stage of diabetes. *BMC Ophthalmol* 2016;16:12.

7 Kim JT, Lee DH, Joe SG, Kim JG, Yoon YH. Changes in choroidal thickness in relation to the severity of retinopathy and macular edema in type 2 diabetic patients. *Invest Ophthalmol Vis Sci* 2013;54(5):3378-3384.

8 Adhi M, Brewer E, Waheed NK, Duker JS. Analysis of morphological features and vascular layers of choroid in diabetic retinopathy using spectral-domain optical coherence tomography. *JAMA Ophthalmol* 2013;131(10):1267-1274.

9 Ho M, Liu DT, Chan VC, Lam DS. Choroidal thickness measurement in myopic eyes by enhanced depth optical coherence tomography. *Ophthalmology* 2013;120(9):1909-1914.

10 Barteselli G, Chhablani J, El-Emam S, Wang H, Chuang J, Kozak I, Cheng L, Bartsch DU, Freeman WR. Choroidal volume variations with age, axial length, and sex in healthy subjects: a three-dimensional analysis. *Ophthalmology* 2012;119(12):2572-2578.

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