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CORRESPONDENCE

Analysis of microaneurysms and capillary density quantified by OCT-angiography and its relation to macular edema and macular ischemia in diabetic maculopathy

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To the Editor:

Optical coherence tomography-based angiography (OCTA) has brought a paradigm shift in the way ophthalmologists are now monitoring and treating patients with diabetic maculopathy. Its ability to analyze the capillary density and microaneurysms (MAs) in different retinal layers/slabs has provided new insight and understanding of diabetic maculopathy [1–3].

One of such report was made by Hsiao et al. [4], where they reported interesting correlation between the visual acuity and macular microvasculature in eyes with diabetic macular edema (DME) with the help of OCTA.

We would like to thank them for sharing their work and also make contributions to their findings based on the results from one of our study, which we believe can help add further knowledge [5].

Our reports are based on OCTA analysis of MAs in diabetic maculopathy for vision-threatening features. The method we used to classify and analyze these MAs are illustrated in Fig. 1 and are based on the principle of "diffractive particle movement detection" used in OCTA.

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MAs have already been characterized as high flow (HF) and low flow (LF) in the literature [2]. However, we have put forward a hypothesis on why it may occur on the first hand. When blood flows through lumens of varying dimensions—such as capillaries with MAs, the flow becomes turbulent and slower. While certain capillaries may recover the flow by compensatory increase in the pressure gradient, others may not. The MAs which achieve higher flows are likely to meet the OCTA threshold and register a signal—hence labeled as HF-MAs. However, due to the increased pressure gradient over an area with pericyte loss, we predict that HF-MAs are prone to leakage and cause macular thickening—especially when located in deep capillary plexuses (DCP). Our study has already illustrated similar results. We found that HF-MAs, which were present in DCP, were likely to be found in areas of macular thickening (71%), with half of them being adjacent to cystoid spaces. Since Hsiao et al. [4] analyzed and reported results based on MAs detected by OCTA, these are HF-MAs. In their results, they also indicate that higher number of these MAs were found in DCP of retinas having DME (Table 1). We conclude that our hypothesis supports both of ours and their findings in relation to HF-MAs and macular edema.

Another interesting finding reported were of the lower density of capillary plexuses (binarized into skeleton density) being associated with poorer BCVA. While the limitation of our study was that we did not evaluate the visual acuity, our study identified LF-MA using enhanced imaging, evaluated their distribution and its relation to the capillary density. We hypothesize that unlike HF-MAs, LF-MAs are result of inadequate or failed compensatory mechanism to upregulate the pressure gradient to maintain flow. While still visible in the fundus photo or other enhanced images, flow rate in such capillaries and LF-MA are inadequate to register a signal in OCTA. This maybe be reflected as decreased capillary density. Hemodynamically, this could be indicative of either sluggish flow or a nonperfusion and could serve as an early warning for an

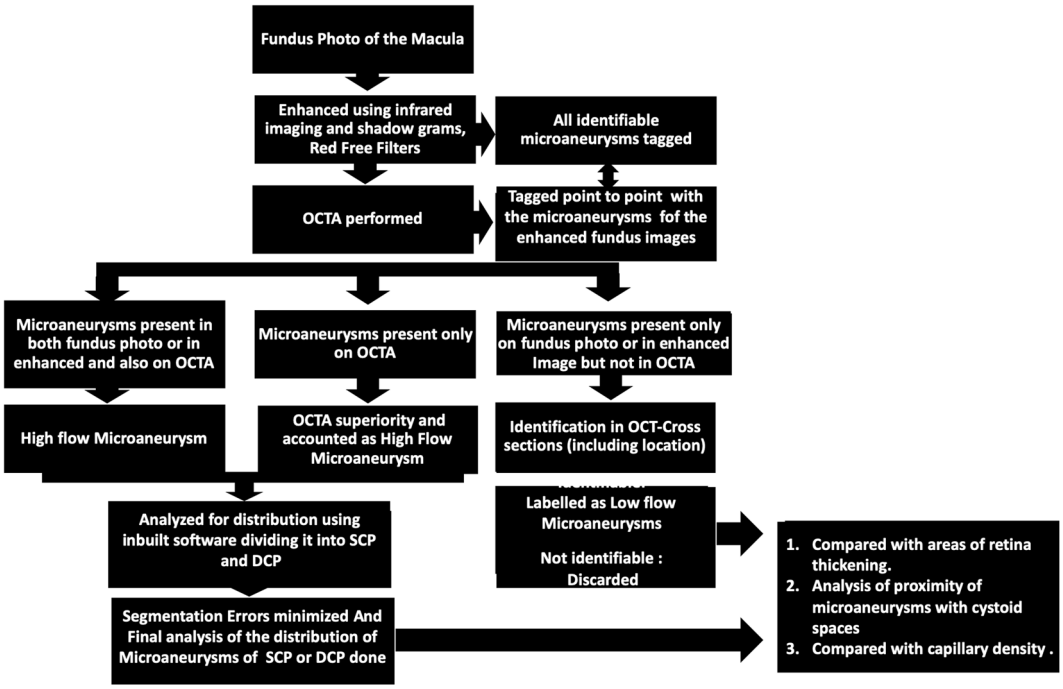

Fig. 1 Identifing microaneurysms. Logical flow diagram illustrating the methods used to classify and characterize microaneurysms in our study.

Table 1 Comparison of findings of Hsiao et al. [4] with our findings.

Octa parameters	Hsiao et al. [4]	Our study
Device	AngioVue system (Avanti OCT; Optovue)	Topcon medical systems—Triton™ DRI PLUS SS-OCT
Type	Split-spectrum amplitude-decorrelation angiography	Swept source
Scanned area	3×3 mm^2	3×3 mm^2
HF in DCP	Mean of 9.8 (4.1 in SCP), all scanned eyes had DME	71.6% of all HF-MAs
HF-MAs in areas of retinal thickening	Not available	60.30%
HF-MAs of DCP in areas of retinal thickening	Higher number in DCP than SCP	71% odds ratio—4.5 ($p = 0.02$)
HF-MAs and cystoid edema	Not analyzed	20% of HF in SCP, 50% of HF in DCP
LF-MAs	Not analyzed	Higher distribution in DCP—72.7% of all LF-MAs
Decreased capillary plexus	Decreased binarization skeleton associated with poorer BCVA, risk of ischemia ($p = 0.03$)	Odds of LF-MAs to be found in areas of decreased capillary densities 25.6 ($p = 0.001$), risk of ischemia
Limitations	Analysis of LF-MA and its distribution not done	Visual acuity not evaluated

impending ischemic maculopathy. Our study supports this hypothesis to a certain extent as we found that the odds of finding these LF-MA in areas of decreased capillary plexus was 25.2 ($p < 0.001$) and nearly 2/3rd of them were also present in the areas corresponding to DCP. Results by Hsiao et al. [4] also supports the finding that the eyes with decreased binarized capillary density (derived from capillary density) were found to have lower BCVA—and could be related to macular ischemia ($p = 0.03$).(Table 1) The authors, however, did not comment on any MAs otherwise visible in fundus photo or other images and were absent in the OCTA hence limiting the scope to correlate their findings adequately with ours.

Irrespective of limitations, this now puts forward an interesting scenario. Retinas with "MAs only" on fundus examination are considered "mild NPDR." But as our results have suggested, MAs need a closer look in terms of flow, location and the capillary density. We believe that these features can help in identifying the eyes "at risk of deterioration" earlier. This now means that the concept of individualized approach for diabetic retinopathy should be thought of in terms of follow-up durations or treatment.

In conclusion, we intend to highlight that the hallmarks of these two papers such as BCVA, HF-MAs, LF-MAs, its locations, capillary density and its relation to macular edema and macular ischemia look interconnected and have lots of future prospect. We recommend that future studies be conducted with combination of all these parameters to further unlock the hidden potential of OCTA. This will

greatly help us to better understand and manage diabetic maculopathy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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