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Reply to Comment on: Retinal and Corneal Neurodegeneration and Its Association to Systemic Signs of Peripheral Neuropathy in Type 2 Diabetes

REPLY

WE WOULD LIKE TO THANK DRS TAKKAR AND TAKKAR FOR their letter and interest in our article.[1]

The authors first comment on our study's finding that even though both corneal and intraepidermal nerve fiber measures decreased in the advanced stages of diabetic retinopathy (DR), there was no statistically significant correlation between them. They suggest that this may be owing to the cranial origin of corneal fibers as opposed to the intraepidermal ones. However, although the corneal fibers derive from the ophthalmic division of the fifth cranial nerve, diabetic cranial neuropathy is known to present as a cranial nerve palsy, mostly either as an oculomotor or facial nerve palsy.[2] The major benefit of using corneal confocal microscopy as a noninvasive technique to detect subclinical small fiber alterations predictive of diabetic peripheral neuropathy (DPN) needs to be emphasized again. Similarly, intraepidermal nerve fiber density, though being invasive, prone to substantial interindividual variability, and specific to the location of biopsy, represents a valuable biomarker of small fiber neuropathy (SFN). Other groups have also found poor correlation of these intraepidermal and corneal signs of neuropathy, where either of them may independently manifest in affected patients, thus promoting a "patchy" pattern of SFN.[3] The precise pathophysiologic mechanisms leading to the different manifestation patterns and the lack of correlation between them are of great scientific interest and definitely merit future investigations prior to selecting one of them as the superior surrogate for DPN.

Further, our study was aimed at defining the extent of inner retinal neurodegeneration in the different stages of DR, and proposes that neurodegenerative changes of the inner retina develop independently of the microvascular alterations defining DR. There is solid evidence that inner retinal neurodegeneration, shown as a selective loss of the retinal nerve fiber layer, ganglion cell layer, and inner plexiform layer thicknesses, plays a pivotal role in the development of diabetic retinal disease.[4] Takkar and Takkar outline that neuronal loss may also affect the "middle retina." Although the "middle retina" is not further defined here, they refer to their previous study,[5] where they used multifocal electroretinography as well as optical coherence tomography (OCT) to evaluate different types of diabetic macular edema (DME). This renders a comparison to our study virtually impossible, as we consciously excluded eyes with DME, as DME represents an entirely different entity of diabetic retinal disease, where the precise segmentation of individual retinal layers in OCT can still be difficult. In particular, it requires meticulous segmentation in order to reveal cases where the presence of intraretinal cysts conceals inner retinal neurodegeneration owing to a consistent central retinal thickness. Whereas Nagesh and associates[5] only assessed the ellipsoid zone and external limiting membrane next to full central macular thickness, they refer to Vujosevic and Midena,[6] who, notably, found an increase rather than decrease in thickness of the inner nuclear and outer plexiform layers in patients with diabetes, which likely represents an activation and hypertrophy of hyperglycemia-susceptible Müller cells rather than neurodegeneration in the "middle retina."

JULIA HAFNER
Department of Ophthalmology and Optometry
Medical University of Vienna
Vienna, Austria
MARKUS ZADRAZIL
Department of Anesthesiology
General Intensive Care and Pain Control
Medical University of Vienna
Vienna, Austria
ANNA GRISOLD
Department of Neurology
Medical University of Vienna
Vienna, Austria
GERDA RICKEN
Institute of Neurology
Medical University of Vienna
Vienna, Austria
MARTIN KRENN
Department of Neurology

Medical University of Vienna
Vienna, Austria
DANIELA KITZMANTL
Institute of Neurology
Medical University of Vienna
Vienna, Austria
ANDREAS POLLREISZ
Department of Ophthalmology and Optometry
Medical University of Vienna
Vienna, Austria
ANDREAS GLEISS
Center for Medical Statistics
Informatics and Intelligent Systems
Medical University of Vienna
Vienna, Austria
URSULA SCHMIDT-ERFURTH
Department of Ophthalmology and Optometry
Medical University of Vienna
Vienna, Austria

CONFLICT OF INTEREST DISCLOSURES: SEE THE ORIGINAL article for any disclosures of the authors.

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Comment On: Predictors of Bubble Formation and Type Obtained With Pneumatic Dissection During Deep Anterior Lamellar Keratoplasty in Keratoconus

EDITOR:

WE READ WITH GREAT INTEREST THE RECENT REPORT BY Scorcia and associates[1] titled "Predictors of bubble formation and type obtained with pneumatic dissection during deep anterior lamellar keratoplasty in keratoconus." The investigators aimed to study the predictors of type 2 big bubble (BB) during BB deep anterior lamellar keratoplasty. They concluded that older age and advanced stages of keratoconus are predictors of type 2 bubble formation during BB deep anterior lamellar keratoplasty, based on their case series of 11 eyes with type 2 BB and 2 eyes with mixed bubble.[1] This study follows our review published in 2015—although not cited in their article—describing risk factors for the formation of type 2 BB in 134 eyes, among which 14 eyes (8 keratoconus and 6 corneal scars) had type 2 BB and 2 eyes with mixed bubble. The mean age for the formation of type 2 BB was 41.9 ± 10.3 years compared with 27.5 ± 9 years for type 1 BB ($P = .001$). Pentacam-based central corneal thickness was statistically significantly lower in eyes with type 2 bubble compared with type 1 bubble ($P = .021$). Our conclusion was that type 2 bubble is more likely to form in elderly patients and those with deep corneal scars and thin corneas.[2]

The authors claim in the third paragraph in the discussion the novelty of the work: "This correlation between age and bubble type occurrence, here reported for the first time, may suggest that the pre-Descemet layer may undergo changes with aging."[1] This is similarly stated clearly in the fifth paragraph in the discussion of our previously published article: "…also old age and scarring may be associated with the structural difference of the pre-Descemet stroma that may not allow easy separation from the overlying stroma." We previously demonstrated the strong correlation between type 2 BB and both old age and the advanced form of stromal diseases.[2]

The authors also highlight the increased risk of double anterior chamber in eyes with type 2 BB, which was first described in another publication by our team[3] and later confirmed by a letter to the editor.[4] To our surprise, the authors cited the letter to the editor (reference 16) as the source of this observation and not the original study.

We would like to congratulate the authors for their well-designed study that confirms our previously published findings.

MOHAMED BAHGAT GOWEIDA
Alexandria, Egypt
MEHRAN ZAREI-GHANAVATI
Tehran, Iran
CHRISTOPHER LIU
Brighton, United Kingdom

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