Re: Hondur et al.: Vitreopapillary findings in nonarteritic ischemic optic neuropathy versus healthy eyes: a clinical and OCT comparison

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TO THE EDITOR: I read with great interest the study by Hondur et al[1] that sought to determine whether there is an association between the vitreopapillary interface and nonarteritic anterior ischemic optic neuropathy (NAION). In this journal in 2015, Drs Parsa and Hoyt[2] published an editorial explaining their rationale for the possibility of the posterior vitreous face playing a role in the development of NAION. Explanations were given based on the effect of vitreous tractional forces on the normal retina and optic disc, but interestingly not on NAION itself; the editorial was, in essence, a medical hypothesis. In fact, Drs Parsa and Hoyt stated, "We welcome efforts using optical coherence tomography and other modalities such as dynamic B-scan ultrasonography to further clarify the role of vitreous separation in the mechanical dynamic stretch injury to a 'disc at risk.'" Since that editorial was published, there have been several studies that have used OCT in an attempt to confirm or refute the hypothesis that mechanical forces generated during the separation process of the posterior vitreous from the optic disc result in NAION.[3]

Hondur et al[1] used a case-control study design to determine whether the vitreopapillary interface in NAION results in perfusion alterations to the optic disc. I commend the authors for their efforts, but it seems to me that their conclusions are not in alignment with the findings, and the study methodology did not allow for a pathway to confirm whether the vitreopapillary interface results in optic disc perfusion defects. There are five points I would like to highlight to support my statement.

First, this was a case-control study that evaluated only one point in time. As mentioned by the authors, posterior vitreous detachment (PVD) is a dynamic process; therefore, a cross-sectional study design will not provide the adequate information needed to determine the mechanical effect of the vitreous interface with the optic disc. A more appropriate method would have been a longitudinal prospective study.

Second, the study did not evaluate patients in the acute stage of NAION, meaning when the optic disc was swollen; therefore, it is not possible to know the status of the posterior vitreous during the active phase of the disease. The authors make the argument that it is difficult to visualize the vitreopapillary interface when the optic disc is swollen, which I humbly disagree with as my personal experience has been the opposite.

Third, a total PVD was not present in 26 of 32 (81%) of NAION eyes. Such a finding would suggest that the vitreous was not separating at the time of the acute event, which would support the notion that the posterior vitreous interface does not play a role in the development of NAION. If one were to believe the vitreopapillary interface played a role in the development of acute NAION, then a PVD should be developing at the time of the acute event and be evident after the event.

Fourth, the 67% of NAION eyes that had apparent epipapillary membranes attached to the optic disc as listed in Table 3 (in the original article) is misleading. That percentage is based on 4 of 6 NAION eyes that had a total PVD, but when calculated from the entire NAION group, the percentage of eyes with epipapillary membranes is only 12.5% (4/32). Furthermore, it is not clear to me that these membranes represent traction as alluded to by the authors and discussed in my fifth and final point.

Fifth, vitreous adhesions—no matter their location, density, and angle—do not equate to vitreous traction. The International Vitreomacular Traction Study Group classified traction as resulting "in anatomic changes in the contour of the foveal surface, intraretinal pseudocyst formation, elevation of the fovea from the [retinal pigment epithelium], or a combination that typically results in reduced or distorted vision. If detectable retinal anatomic changes occur on OCT, with concurrent vitreous status showing perifoveolar PVD, the eye is characterized as having VMT."[4]

I as well as others believe that in some patients the mechanical forces generated during epipapillary vitreous separation leads to mechanical distortion of the superficial optic disc blood vessels causing disruption of blood flow resulting in a subtype of anterior ischemic optic neuropathy that should be termed vitreopapillary traction optic neuropathy (VPTON), which is a distinct entity from NAION.[5]

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REPLY: We thank Dr Bhatti for his comments about our article.[1]

First, the generation of anteroposterior tractional forces on the optic nerve during posterior vitreous detachment (PVD) has been reported in different ocular pathologies, including nonarteritic anterior ischemic optic neuropathy (NAION). However, the link between vitreopapillary traction and crowded discs has not been established. We aimed to fill this gap and provide insights into what makes crowded discs more prone to develop NAION and why NAION does not develop in all crowded optic discs. We found no difference in the PVD rates over the macula among patients with NAION vs 2 other control groups; however, we found that the hyaloid remained attached to crowded discs at a higher rate. Although persistent attachment of the hyaloid to the optic nerve head after separation from the macula suggests relatively stronger attachment to crowded discs, we do not claim that more robust vitreopapillary traction over the disc is the only reason for NAION. A careful reading of the article reveals that one critical difference between the discs that develop NAION and the controls is the number of focal vitreopapillary attachments and their proximity to optic nerve head vasculature, as shown in Figs 1 and 4 (in the original article). The direct and more pronounced transmission of vitreopapillary traction on optic nerve vessels may trigger a pathological response, leading to vascular endothelial dysfunction or vasospasm similar to what was reported in the literature.[1]

The significant limitation of conducting prospective NAION trials is its low incidence (2−10 cases per 100 000 persons in the United States), which makes our cohort represent 320 000−1 600 000 people. However, we conducted our study meticulously to ensure the reliability and validity of our findings. In a few cases, we could follow and document the impact of focal vitreopapillary attachments during the development and resolution of PVD and NAION (Fig 4 in the original article).

Second, we observed the impact of focal vitreopapillary adhesions on a crowded disc during different stages of NAION (Fig 4 in the original article). We agree that secondary pathologies, such as optic nerve head swelling and hemorrhages, during NAION's acute phases may make it difficult to interpret the images.[2] We mentioned this difficulty to point out that attempts to study the impact of PVD on NAION should not use total acute PVD as an outcome for determining the presence of PVD, because more tractional forces will be expected during ocular saccadic movements once the vitreous separates from the macula but remains attached to the disc.

Third, posterior hyaloid separation from the macula but its attachment to the crowded optic nerves is a critical finding of our study. This allows all the anteroposterior tractional forces to be directed toward the optic nerve head. Numerical simulations on the eye models indicate the generation of large tractional forces on the tissues close to the vitreous attachment points in such conditions.[3] A well-known example is the vitreomacular traction syndrome. In incomplete PVD, tractional forces created by the saccadic eye movements act on smaller areas and generate increased tractional pressures considering the relationship between the pressure (P), force (F), and area (A) ($P = F/A$). Thus, unlike Dr Bhatti, we believe the higher rates of incomplete PVD overcrowded discs supports the role of vitreopapillary traction in triggering the events leading to NAION in such discs. Yet, we also showed that anatomical differences explain why some crowded discs develop NAION in the setting of vitreopapillary traction.

Fourth, cortical vitreous patches remain attached to the inner retina at points where the gel is firmly adherent.[4] A higher rate of remnant vitreous on the discs in NAION than in the healthy controls indicates firmer adhesion of the cortical gel on the NAION discs. Thus, including patients with NAION and controls who had not developed PVD in such a comparison would not be appropriate.

Fifth, we believe we displayed anatomical changes in the optic nerve structure with traction accurately (Fig 4 in the original article), similar to those previously reported.[5] As referenced by Dr Bhatti, the description accepted for vitreomacular traction applies to "vitreomacular traction," not "vitreopapillary traction." Structural and biophysical differences exist in both tissues; what is valid for one may not be accurate for the other.

Again, we thank Dr Bhatti for his interest and valuable comments.

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