Author Response: Choroidal Thickness Change after Water Drinking Is Greater in Angle Closure Than in Open-Angle Eyes

We thank De Moraes et al.¹ for the opportunity to emphasize the findings of our study and how they differ from their publication.² We reported, for the first time, the response of angle closure (AC) patients to the water-drinking test (WDT), including changes in IOP, blood pressure (BP), and choroidal thickness.³ The most important finding was that AC eyes significantly increase choroidal thickness in the WDT, whereas open angle glaucoma (OAG) eyes do not. In addition, a shallowing of the anterior chamber was observed in AC but not in OAG eyes, illustrating how thickening of the choroid can hypothetically intensify pupil block and make AC more likely. Our findings further support the concept⁴ that dynamic choroidal thickness change is a contributing feature to AC disease. AC eyes not only have greater choroidal expansion than other eyes, but their resting choroidal thickness is greater than that of OAG or control eyes,⁵ including in the anterior choroid,⁶ after adjusting for relevant variables like age, axial length, and IOP. The references that the letter by De Moraes et al.¹ cites from Lowe⁷ and from Kirsch⁸ neither suggested nor documented with data any study of choroidal thickness, and neither mentioned choroidal participation in AC.

The fact that IOP increases without a commensurate choroidal thickness increase in OAG eyes supports the hypothesis that increased outflow resistance is the general mechanism of IOP rise after WDT.⁹⁻¹¹ This contradicts the conclusion of De Moraes et al.² that the IOP rise in the WDT is due to choroidal expansion. For OAG eyes in which impaired outflow resistance is relevant, the usefulness of the WDT as a risk factor has been documented.¹² Among our patients, the individual increase in choroidal thickness after WDT was too small to provide adequate positive predictive power to identify AC suspects with sufficient risk to merit iridotomy. Further study is merited to find methods to provoke choroidal thickness change as a diagnostic maneuver.

De Moraes et al.² attempted to measure choroidal thickness by ultrasound, which admittedly has a resolution too low to detect the small changes in choroidal thickness seen in our work and that of many other authors using optical coherence tomography (SD-OCT). They assumed that by measuring the distance from the inner retina to outer sclera at one single point that a change in "choroidal thickness" could be estimated by the change in the overall thickness of the retina/choroid/sclera. It is this combined thickness that they report as "ChT" (1000 μm at baseline). Ironically, they fault our method as limited, although we measured actual mean choroidal thickness throughout a much larger, 6-mm-wide zone, rigidly controlled to be at the same position in repeated images during the WDT, and using a method with more than 10 times greater accuracy. Their comment that the choroid might expand more in one area than another during these conditions is not supported by any data. The shape of large, clinically visible choroidal detachments is a totally different situation and not relevant to this discussion. De Moraes et al.¹ cite Esmaeelpour et al.¹³ to support their claim that "choroidal thickness varies significantly in different areas of the posterior pole, being particularly thicker in areas farther from the fovea." Esmaeelpour et al.¹³ actually state: "For all eyes, the mean $\pm$ SD of ChTs were 315 $\pm$ 106 μm (Central), 250 $\pm$ 113 μm (Nasal), 276 $\pm$ 95 μm (Temporal), 315 $\pm$ 112 μm (Superior),

and 293 $\pm$ 106 μm (Inferior)." So, De Moraes et al.² have incorrectly written that the choroid is thicker more peripherally. Our SD-OCT method, as reported, measures choroidal thickness in the full range of 25 to 30 degrees centered on the fovea, as in Esmaeelpour et al.,¹³ and our mean choroidal thickness data thus take into account the variation of up to 20% thinner choroidal thickness at the periphery of this zone compared with the fovea. Likewise, De Moraes et al.'s¹ statement: "The authors [Esmaeelpour et al.¹³] reported an increase in thickness of approximately 1500 μm inferior to the center of the fovea" is incorrect in two ways. As seen previously, when considering all eyes, the inferior choroidal thickness was found to be not thicker, but thinner than mean foveal choroidal thickness, and only by a mean of 22 μm , not 1500 μm . Furthermore, their use of the phrase "increase in thickness" suggests a dynamic change, whereas the cited work compared static choroidal thickness in different regions, not a change, as we studied after WDT.

Even if we accept the assumption that the single point, ultrasound measurement, by De Moraes et al.² could estimate change in choroidal thickness from the change in the whole eye wall thickness, Figure 4 in their data indicates that the mean "ChT" rose from 1000 μm to 1700 μm and the text states, "the mean ChT increased from 1.03 $\pm$ 0.12 mm to 1.23 $\pm$ 0.19 mm ($P < 0.001$)." We therefore correctly quoted their assertion that the change in choroidal thickness was 200 or more microns after WDT. Even in our AC group, the mean choroidal thickness increase by SD-OCT was only 4 μm (statistically significant). The eye has a relationship between IOP and volume that has been documented from the time of Friedenwald and in more recent data from cannulated, living human eyes, as summarized by Silver and Geyer.¹⁴ Using the mean values of the pressure-volume relationship, we see that if the choroidal thickness increased quickly by 700 or even by 200 μm , the IOP would be astronomically higher than mean BP. This calculation is done by simple solid geometry, assuming the measured baseline choroidal thickness, a choroid occupying the posterior two-thirds of the globe circumference, and uniform choroidal expansion, with the difference between baseline and expanded choroidal volume equal to the volume change that generates a theoretical IOP rise. We provided the details to perform this calculation within our article and note that the letter writers had no difficulty in performing the calculation themselves.

Further, while they question our WDT technique, the average IOP rise in standard WDT is 5 mm Hg, which is exactly what we observed. Thus, our failure to find a large increase in choroidal thickness was not a result of failing to produce IOP elevation or using a slight variation in methodology. We also note that we tested three times as many subjects as De Moraes et al.² (90 persons compared with 30) and that our data are quite compatible with past ophthalmic and systemic literature on WDT, including the concomitant rise in BP.

Choroidal thickness varies with both BP and IOP, as we and others have documented by SD-OCT, thus diurnal variation in these parameters would lead to potential changes in choroidal thickness. But, as opposed to the relatively acute changes during a WDT, diurnal shifts in IOP and BP that change choroidal thickness would occur more slowly, allowing outflow of aqueous anteriorly to modulate the resultant IOP level.

With increasingly precise techniques and modern concepts suggesting that there are multiple contributing features to AC disease, we and our colleagues can hopefully concentrate on

forward-thinking approaches to improve diagnosis and treatment.

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