The paper that Borgohain and associates referenced to support their argument reported outcomes of secondary glaucoma following vitrectomy.[3] Thirty-nine percent of their cohort had intravitreal silicone oil and 11% of eyes had extensive peripheral anterior synechiae or neovascularization. In other words, their cohort represented the types of patients we meticulously excluded. As we stated in the Discussion section of our paper, a secondary cause of glaucoma could not be attributed to our cohort based on existing knowledge. However, we postulated that, with increased understanding of the pathophysiology in these patients, "glaucoma following vitrectomy" will become a recognized entity among the causes of secondary glaucoma.

Concerning the issue of mean baseline IOP being a risk factor for the development of glaucoma, it is important to note that the patients included in the study did not have elevated baseline pressures. The mean baseline IOP among the cohort developing POAG, or POAG and POAG suspect, was 16.9 ± 2.5 mm Hg and 16.3 ± 2.7 mm Hg (mean ± standard deviation), respectively. The mean baseline IOP of the operative cohort as a whole was 15.2 ± 3.2 mm Hg.

With respect to the issue of steroid use, we agree that IOP rise can occur within 1–2 weeks of initiating therapy, and therefore all patients developing elevated IOP while on steroids were excluded from the study. Out of an abundance of caution, we also excluded patients who used steroids for an extended period of time, defined as 2 or more months (18 patients overall, Figure 1[1]). Prolonged steroid use after vitreoretinal surgery is often recommended when there is ongoing inflammation, and the intent was to minimize confounding from glaucoma associated with inflammation or its treatment. However, excluding all patients receiving steroid eye drops for 1–2 weeks would be impractical, as this would include most postoperative patients, and a cut-off of 2 months was felt to be more reasonable.

We thank Borgohain and associates for their interest in our paper and the opportunity to clarify some key points.

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REFERENCES

1. Mansukhani SA, Barkmeier AJ, Bakri SJ, et al. The risk of primary open-angle glaucoma following vitreoretinal surgery—a population-based study. *Am J Ophthalmol* 2018;193(9):143–155.
2. Prum BE Jr, Rosenberg LF, Gedde SJ, et al. Primary Open-Angle Glaucoma Preferred Practice Pattern((R)) Guidelines. *Ophthalmology* 2016;123:P41–P111.
3. Tranos P, Asaria R, Aylward W, Sullivan P, Franks W. Long term outcome of secondary glaucoma following vitreoretinal surgery. *Br J Ophthalmol* 2004;88:341–343.

Predictive Factors of Response to Mineralocorticoid Receptor Antagonists in Nonresolving Central Serous Chorioretinopathy

REPLY

WE THANK DRS DAN AND MIHAI CĂLUGĂRU FOR THEIR interest in our work.[1] However, we would like to clarify some of the points they raised.

We agree that our study has a retrospective design with missing data. Nevertheless, it is incorrect to state that "34% of eyes were lost to follow-up." As described in the methods section, patients with complete resolution of serous retinal detachment at 3 months were treated for only 3 months and were not included in the analysis at 6 months. All missing data and number of studied eyes are precisely written in each table.

However, we acknowledge the high rate of missing data for optical coherence tomography (OCT) angiography. Indeed, we included patients from 2012 to 2016 and the OCT angiography machine was available in our hospital in 2015. All choroidal neovascularization (CNV) detected in our study were type 1 CNV. Our results are in line with the study by Sacconi and associates[2] showing that the presence of CNV is a factor of poor response to treatment. Thus, we agree that the difference between both groups in our study is not statistically significant, probably because of the small sample size. This limitation is identified in the discussion section of our paper.

We also agree that corticosteroid intake could be a factor of poor response to treatment, but it did not reach statistical significance in the multivariate analysis. We thank the authors for their insight into the possible role of corticosteroids related to the mineralocorticoid receptor pathway hypothesis.

Furthermore, the authors focus on the lack of extensive characterization of retinal imaging. We agree that analyzing OCT parameters such as the retinal pigment epithelium status or the line of photoreceptor cells would have been interesting for predicting treatment response and may be a suitable outcome for future analyses. We analyzed several established parameters including central macular thickness, subretinal detachment height, and

choroidal thickness (subfoveal, 1000 μm nasal and temporal to the fovea).

In addition, the authors raised a concern about systemic data not presented in our study. Our study was conducted in a real-world, clinical setting. As stated in the methods section (treatment protocol), all patients had blood testing including kalemia and creatininemia at baseline and during the follow-up. However, we did not routinely evaluate endogenous cortisol (neither the type A personality nor *Helicobacter pylori* infection).

Finally, although the study is limited by its retrospective design, it offers clinically relevant insights and potential predictive factors for treatment response. Obviously, further prospective studies are needed to confirm these factors.

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REFERENCES

1. Bousquet E, Dhundass M, Lejoyeux R, et al. Predictive factors of response to mineralocorticoid receptor antagonists in nonresolving central serous chorioretinopathy. *Am J Ophthalmol* 2018; https://doi.org/10.1016/j.ajo.2018.09.034.
2. Sacconi R, Baldin G, Carnevali A, et al. Response of central serous chorioretinopathy evaluated by multimodal retinal imaging. *Eye (Lond)* 2018;32(4):734–742.

Predictive Factors of Response to Mineralocorticoid Receptor Antagonist in Nonresolving Central Serous Chorioretinopathy

EDITOR:

WE WOULD LIKE TO ADDRESS SEVERAL ISSUES WITH THE study of Bousquet and associates.[1]

The study had a retrospective design and a short follow-up duration, with a fairly high proportion of eyes lost (34.37%) until the end of the follow-up period. Moreover, the measurements of the subfoveal choroidal thickness and the optical coherence tomography angiography (OCTA) images were not available in 27.11% and 23.72% of patients, respectively.

Two causes might explain the pretty high percentage of nonresponder patients (33.89%), namely, the corticosteroid intake and the choroidal neovascularization (CNV) detected by OCTA.

There was a significant difference regarding the previous or ongoing corticosteroid intake between patients in the nonresponder and responder groups (61.1% and 38.3%, respectively). Systemic corticosteroids have been associated with occurrences, prolongation, exacerbation, and recurrences of central serous chorioretinopathy (CSC) resulting in the paradoxical pro-edematous effects of glucocorticoids in CSC. Importantly, inappropriate or excessive activation of the mineralocorticoid receptor pathway involved in the development of CSC in ocular cells by the glucocorticoids can favor or even trigger the accumulation of subretinal fluid in CSC patients instead of acting on its absorption, as observed in macular edema of other origins. The molecular mechanisms include expression of the calcium-dependent potassium channel (KCa2.3) in the endothelium of choroidal vessels, inducing subsequent vasodilation with choroidal thickening.[2,3]

Nothing was stated referring to the types of CNV encountered in this series, namely, the type 1 located under the retinal pigment epithelium (RPE), the type 2 located in the subretinal space, or the type 3 intraretinal, attesting the existence of the neovascular CSC. The difference concerning the percentages of the neovascular CSC between patients in the responder and nonresponder groups (5.9% and 25%, respectively) was obvious but insignificant. Of note, the OCTA images for the detection of the neovascular CSC were not available in 23% and 25% of patients in the responder and nonresponder groups, respectively. The CNV might be considered as a factor of poor response to treatment with the mineralocorticoid receptor antagonists by preventing them from reaching and binding to the structurally similar mineralocorticoid and glucocorticoid receptors.

The qualitative status of the RPE band–Bruch membrane complex (which is primarily involved in the nonresolving CSC and has a contribution in the CSC pathogenesis), and grading of the RPE changes (serous pigment epithelial detachment, pigment migration within the neurosensory retina, RPE porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE hypertrophy, and diffuse or scattered leakage points through the RPE on fluorescein angiography), were not documented in the study groups.

There were no data in patients of the 2 study groups on the multimodal imaging of the overlying photoreceptor cell layer, which may suffer progressive and irreversible damages in cases of the chronic CSC because of the persistence of the subretinal fluid caused by pronounced dysfunctional RPE outer blood–retinal barrier. These alterations include outer nuclear layer thinning, external limiting membrane band disruption, discontinuity of the ellipsoid zone, elongation of the photoreceptor outer segments, interdigitation zone loss,