Dr Chawla underlined the fact that the same issues might also affect decorrelation signal analysis, and we agree. This is the reason why all imaging data should be carefully interpreted and supported by histologic validations, as declared in our paper. Taking into account all these considerations, we can assert that the same above-described observations may also be applied to this potential issue. In addition, we believe that all the technical pitfalls listed by Dr Chawla do not represent a negative criticism limited to our work, since the same "risks" can also be run by the hundreds of papers using the largely adopted "Vessel Density" parameter to quantify vascular impairment.

With respect to the "unanswered question" regarding the induction of retinal vascular changes from a choroidal disease, we would like to highlight some points. Firstly, CNV pathogenesis is getting more and more complex, owing to the new discoveries and technological advances. Indeed, both in papers and in scientific meetings, some researchers have already started to replace the traditional CNV definition with a newer one, namely macular neovascularization, in order to emphasize that the onset and progression of neovascular growth can no longer be ascribed only to the choroid. Furthermore, looking at the alterations of the fellow eye, we would like to point out that our findings further support the view of retinal vascular changes as key signs of age-related macular degeneration (AMD). These alterations may lead to a different classification of the neovascular AMD stage and also potentially to a different prognostic outcome toward the atrophic macular changes. From our point of view, our study had the merit to try to convert into quantitative metrics the largely qualitatively reported vascular changes occurring in AMD. Of course, we consider it unlikely that a single, cross-sectional study may account for a global characterization of a complex manifestation like AMD-related CNV. Further investigations are warranted to correlate OCTA parameters and clinical course and response to therapy. We are working on this topic, following up our patients, and we hope to provide the results of our investigations soon.

With respect to Dr Chawla's comment regarding the adopted threshold, we believe that our Methods description was considerably misunderstood. Indeed, we adopted a "mean" threshold to binarize images, namely a standard approach provided by ImageJ. As described in several previous papers, this represents a good way to select vascular signal from segmented images.

Regarding the lack of representative CNV images, we deliberately decided not to submit an additional figure, since in our opinion—and evidently in the opinion of the reviewers—this would not have added significant, qualitatively appreciable information.

All the above-discussed points highlight that OCTA is a powerful tool, although not devoid of artifacts or misinterpretations. For this reason, we strongly recommend, first of all to ourselves, and to researchers adopting this kind of approaches, to always consider the current methodology limits and to base their conclusions only on the mere data, avoiding excessive speculations or overinterpretation of their results. As suggested by Dr Chawla, an international consensus for the use of OCTA is needed to establish a standardized guide to the analysis of OCTA data.

In conclusion, we totally agree with Dr Chawla's suggestion to perform prospective interventional studies to expand the available information. However, as declared in the Limitations, our study was designed as a cross-sectional feasibility investigation, testing new quantitative approaches for the analysis of OCTA data. Therefore, all other aspects were beyond the main scope of our present work and will need further investigation.

ALESSANDRO ARRIGO
FRANCESCO ROMANO
FRANCESCO BANDELLO
MAURIZIO BATTAGLIA PARODI
Milan, Italy

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

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Use of Autologous Serum Tears for the Treatment of Ocular Surface Disease From Patients With Systemic Autoimmune Diseases

EDITOR:

WE READ THE RECENT STUDY BY ALI AND ASSOCIATES.[1] THE article addressed an interesting topic, but there are some drawbacks, as outlined below.

First, in the assessment of subjective and objective improvement after using autologous serum tears (AST), there is no analysis to show the effect of confounding factors of other topical and systemic drugs mentioned in Tables 1 and 2, especially systemic immunosuppressive medication, topical cyclosporine, and steroids that all patients did not receive.

The second fact is the neglected role of omega-3 fatty acid products[2]; it is not clear if they were prescribed before AST or if they were not used at all because of their controversial role in production deficiencies like Sjögren syndrome.[2]

Third is the role of tarsorrhaphy in the severe dry eye; the authors did not discuss tarsorrhaphy in their patients. This is one of our usual procedures, especially for the severe dry eye.[2] Our question regards how many patients underwent tarsorrhaphy before receiving AST. How did they manage the confounding effect of tarsorrhaphy in these patients?

Fourth, the authors included different systemic diseases with different pathophysiology and management like Sjögren syndrome and mucous membrane pemphigoid. We would like to ask whether there was any subgroup analysis in this setting.

Fifth, they compared the percentage of patients with punctate epithelial erosion, filamentary keratopathy, and corneal epithelial defects. In this sample size with 51 patients, a "before- and after-treatment" analysis of tear break-up time, aqueous tear production (Schirmer test), fluorescein clearance test, or tear function index works better rather than reporting and comparing the percentage of patients with each finding.

Sixth, there is no subgroup analysis to show the effect of increased concentrations of AST in some patients on final results.

MOHAMMAD SOLEIMANI
SEYED ALI TABATABAEI
RAZIEH MAHMOUDZADEH
Tehran, Iran

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Stroke Risk and Risk Factors in Patients With Central Retinal Artery Occlusion

EDITOR:

WE READ WITH INTEREST THE RECENTLY PUBLISHED article[1] and commentaries[2,3] on the stroke risk and acute management of patients with central retinal artery occlusion (CRAO). As emphasized by Lavin and associates,[1] CRAO patients have a high risk of stroke and cardiovascular events. In Lavin and associates' series of 103 patients with acute CRAO seen within 7 days of onset of visual loss, 37.3% of the 67 patients with brain magnetic resonance imaging had coincident acute strokes, 36.7% of patients had severe carotid disease (greater than 70% stenosis, dissection, or intra-arterial thrombus), 33% presented with hypertensive emergency, and 20% had a myocardial infarction or severe cardiac disease. Urgent evaluation of these patients by stroke neurologists and ophthalmologists in the emergency department resulted in rapid surgical intervention in 25% of patients and a change in medication in 93% of patients. Death occurred prior to the 2-year follow-up in 8% of CRAO patients, emphasizing the severity of systemic diseases associated with CRAOs.

These results are similar to those of recently published studies (see reference 4) and clearly highlight the need to expedite the evaluation and treatment of CRAO patients. Unfortunately, this is still a matter of some debate in the United States and many ophthalmologists continue to delay this process by not sending acute CRAO patients immediately to an emergency department affiliated with a stroke center.[4,5] Indeed, it is critical that the cause of CRAO be quickly and accurately identified in order to allow for appropriate secondary stroke prevention (which may require urgent surgical intervention) based on the mechanism of CRAO.

Despite a large body of literature supporting urgent evaluation of all acute CRAO patients by stroke neurologists, and the demonstrated value of cerebral imaging even in the absence of any neurologic symptoms, Dr Hayreh[2] continues to question the necessity of involving neurologists in the workup of CRAO patients. Urgent evaluation in an emergency department affiliated with a stroke center is not "controversial." Rather, it is standard of care, as recommended by the American Heart Association and the American Stroke Association.[4,6]

A stroke workup is indeed expensive and needs to be guided by experts who will be able to immediately handle complications and decide whether costly treatments or interventions should be prescribed. Enormous progress in the understanding of stroke and prevention of devastating neurologic and cardiovascular complications has occurred within the past 20 years. Stroke is now a recognized neurologic specialty that requires a specific fellowship. The fact that Dr Hayreh suggests that ophthalmologists can do as well as stroke neurologists in the evaluation of CRAO patients is unsettling. As emphasized in Dr Arnold's commentary,[3] the paradigm for management of acute retinal ischemia has changed. Dr Hayreh's approach is outdated and potentially dangerous. Ophthalmologists should continue to practice ophthalmology and leave cerebrovascular diseases to stroke neurologists. Eye care providers play an essential role in evaluating patients with acute visual loss urgently and by making the correct diagnosis of acute retinal ischemia. Once the diagnosis is established, they should follow existing guidelines and send these patients