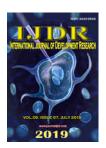


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RESEARCH ARTICLE

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LOSS OF PEAK VISION IN RETINAL VEIN OCCLUSION PATIENTS TREATED FOR MACULAR EDEMA

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ABSTRACT

The authors are commenting on the article entitled "Loss of peak vision in retinal vein occlusion patiets treated for macular edema" published by Iftikhar *et al.* in *Am J Ophthalmol* 2019; 205(September):17-26. After thorough analysis of the issues related to the central retinal vein occlusions, the authors concluded that the central/hemicentral retinal vein occlusion has to be considered an ophthalmic emergency. Therefore, therapy with anti-vascular endothelial growth factor agents has to be promptly applied as soon as possible after central retinal vein occlusion onset. Regardless of the antiangiogenic agents chosen, the treatment paradigms used (e.g., treat-and-extend, pro re nata, fixed-interval, or escalated algorithm), the patient age, the baseline best-corrected visual acuity, and the type of occlusion (ischemic/nonischemic form), the efficacy of treatment depends primarily on the promptness of the therapy after central/hemicentral retinal vein occlusion onset, which can be considered a key driver predicting visual and functional future outcomes.

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INTRODUCTION

The study by Iftikhar *et al.* (2019) evaluated long-term visual and anatomic outcomes in patients with retinal vein occlusion (RVO) treated with anti-vascular endothelial growth factor (VEGF) agents. We would like to address several issues related to the patients with central retinal vein occlusions (CRVO) included in this study.

Although the study had a prospective design and a long-term follow-up for CRVO patients (78 months), the proportions of patients lost until they reached the peak and final visions were fairly high (12.5% and 65%, respectively), which influenced the aggregate data and might cause an inadvertent bias. Furthermore, standard care consisted of a pro re nata (PRN) regimen with anti-VEGF agent initially, but over time many patients were transitioned to a treat-and-extend protocol and those who showed poor responsiveness to anti-VEGF injections were converted to a dexamethasone implant (Ozurdex, Allergan, Irvine, California, USA). Taken together, these findings may have confounded the results.

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Nothing was stated referring to the grouping of the CRVO occlusions in the 2 types (ischemic and nonischemic occlusions) having definitely different pathogenesis, clinical features, prognoses, and management.

Likewise, there were no data with regard to the CRVO-associated comorbidities depending on the age of the patient, that is, the common systemic conditions such as hypertension and diabetes in patients older than 50 years and the hyperviscosity syndrome or inflammatory condition in patients less than 50 years of age. The CRVOs belonging to both groups of age have completely different prognoses (Călugăru *et al.* 2017).

There were no data on the length of time between symptom onset and examination of the eye/initiating anti-VEGF treatment, which should have subdivided the CRVOs into the following three stages: the early acute stage of the disease when the eye was examined within 90 days, the intermediate stage when it was examined 91-365 days after occlusion onset, and the late stage when the examination of the eye was performed more than 1 year since the onset of venous occlusion (Hayreh *et al.*1990).

There is a great discrepancy between the data exhibited in the Table 1 and those inferred by us from the Figure 1C regarding the letter scores of the mean baseline, peak, final, and

differential (peak – final) best-corrected visual acuities (BCVA), namely 48, 74, 56, and 22 letters, respectively, shown in the Table 1 and 48, 62, 50, and 12 letters, respectively, displayed in the Figure 1C. Which of them are correct? Likewise, the BCVA loss for CRVO patients (peak – final) is 18 letters as shown in the abstract and not 22 letters as shown in the Table 1.

The following relevant data are missing in the study: the type of anti-VEGF agent used and the schedule of treatment; the assessment of the macular ischemia; the existence or not of the disorganization of the retinal inner layers and its severity (mild, severe, and severe with damaged ellipsoid zone [EZ]); the optical coherence tomography patterns of the macular edema (diffuse/subretinal fluid/cystic changes/mixed type) and the location of the intraretinal cystoid fluid (ganglion cell layer/inner or outer nuclear layers); the damages of the photoreceptor cell layer (thinning of the outer nuclear layer/external limiting membrane band defect/EZ disruption, interdigitation zone loss); the changes of the retinal pigment epithelial band-Bruch membrane complex (pigment migration within the neurosensory retina, retinal pigment epithelium [RPE] porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE thickening); the proportions of the patients with ocular hypertension, cardiovascular and cerebrovascular diseases, obesity, hyperviscosity syndromes, and inflammatory conditions; the proportion of the patients who developed neovascularization (Călugăru et al., 2018).

The final results of this study were poor. Specifically, 75% of CRVO patients required anti-VEGF injections to control edema within 6 months of their last visit, indicating that they were not yet stable, and only 20% of them had edema resolution. The results of our 3-year prospective clinical study (Călugăru et al., 2015) regarding bevacizumab (Avastin; Genentech, Inc., San Francisco, California, USA) treatment in patients with acute central/hemicentral RVOs (≤ 1 month after the occlusion was diagnosed) were far better than those of the present series. They substantiated, for the first time, evidence suggesting that early treatment applied immediately after the clinical onset of the venous occlusion provided significant and sustained improvements in BCVA and foveal thickness with inactive disease (dry retina and stable BCVA for at least 6 months after the last injection) in most phakic patients (91.22% of the cases), making this treatment option a rational and viable therapeutic strategy.

Altogether, the central/hemicentral RVO has to be considered an ophthalmic emergency (Călugăru *et al.*, 2015a). Therefore, therapy with anti-VEGF agents has to be promptly applied as soon as possible after CRVO onset. Regardless of the antiangiogenic agents chosen, the treatment paradigms used (e.g., treat-and-extend, PRN, fixed-interval, or escalated algorithm), the patient age, the baseline BCVA, and the type of occlusion (ischemic/nonischemic form), the efficacy of treatment depends primarily on the promptness of the therapy after CRVO onset, which can be considered a key driver predicting visual and functional future outcomes (Călugăru *et al.* 2017, 2018).

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