

OCT evaluation as a prognostic indicator for management of macular edema secondary to venous occlusion treated with Ranibizumab

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Research Article

Keywords:

Posted Date: September 29th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10548635/v1>

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Additional Declarations: No competing interests reported.

Abstract

Aim: To study OCT characteristics as a prognostic guide in macular edema secondary to non-ischemic central retinal vein occlusion treated with intravitreal Ranibizumab

Materials and methods: 60 patients with macular edema secondary to non-ischemic central retinal vein occlusion treated with Ranibizumab

OCT analyzed on pattern of macular edema, reflectivity of outer band of photoreceptor-RPE complex. Its bearing on visual prognosis was analyzed.

RESULTS:

Good reflectivity of outer layer is a good prognostic feature.

Cystoid pattern is a better prognostic indicator than sub retinal fluid

Conclusion: The type of macular edema and reflectivity of third high reflectivity band before treatment can be predictive of visual outcome

INTRODUCTION:

With a prevalence of 0.7 – 1.6%, retinal venous occlusions (RVO) form the second most common retinal vascular diseases, following diabetic retinopathy. Macular edema is one of the major causes for vision loss in various types of retinal vein occlusions. Anti-vascular endothelial growth factor (Anti-VEGF) agents namely Bevacizumab (Avastin), Ranibizumab (Lucentis) and Aflibercept (Eylea) have been reported to be efficacious in treating macular edema.

*(*Ophthalmology volume 113, number 3, March 2006, page – 363- 372)*

*(*Retina, 2007, volume 27, number 4, page – 419 – 425)*

Following resolution of macular edema after successful treatment, most patients have satisfactory visual recovery. However, some patients have a poor visual outcome despite complete resolution of the macular edema.

*(*Retina, 2007, volume 27, number 4, page – 426 – 431)*

Optical coherence tomography (OCT) is an effective tool for measuring quantitative and qualitative parameters of the macula, such as central macular thickness, intraretinal abnormalities and the reflectivity from vital layers of the retina namely the Internal limiting membrane (ILM) and Retinal pigment epithelium (RPE – photoreceptor) complex.

*(*AJO – Volume 1, January 2006)*

(*BJO – 2007, 91, 1644-1649)

Patients who were posted to undergo Intravitreal Ranibizumab for macular edema secondary to non-ischemic central retinal vein occlusion were included. The OCT findings were analyzed to assess the visual potential in these patients.

METHODS:

Retrospective study to evaluate the OCT patterns to determine the prognostic factors for visual recovery secondary to treatment of macular edema in non ischemic venous occlusion with intravitreal injection of Ranibizumab (0.5 mg in 0.05 ml)

The characteristics features on OCT evaluated are:

1. Type of edema – Cystoid macular edema (CME) or subretinal fluid (SRF).
2. Reflectivity from third high reflective band (HRB) corresponding to the RPE – photoreceptor complex.
3. Central macular thickness (CMT).

Definitions:

CME: Hyporeflective intraretinal cavities radiating from the center of the macula

SRF: Posterior surface of retina elevated above the Retinal pigment epithelium.

Good HRB: Good reflectivity from RPE-photoreceptor layer as compared to non edematous area

Poor HRB: Poor reflectivity from RPE-photoreceptor layer as compared to non edematous area

CMT: Distance between the inner retinal surface and Retinal pigment epithelium (including subretinal fluid if present).

PATIENTS:

A total of 61 eyes of 60 patients of macular edema secondary to non-ischemic central retinal vein occlusion were studied.

Inclusion criteria were the presenting visual acuity was more than 6/60 on Snellen's visual acuity chart. The patient's age was above 18 years. No evidence of any retinal ischemia or any retinopathy on presentation. Only naive patients, who did not receive any form of treatment before, were included in the study.

Exclusion criteria were the best corrected visual acuity was less than 6/60 at the time of presentation. The presenting age was less than 18 years. Any foveal hemorrhage at presentation was not included. Any evidence of macular ischemia on fluorescein angiogram or the presence of extensive capillary non perfusion areas on fluorescein angiogram was not included in the study. The presence of any other retinopathy which could have contributed to the macular edema was not included. Any history of previous retina treatment either by laser or intravitreal injection or retinal surgery were excluded from the study. On follow up if there is any evidence of conversion of the vein occlusion from non-ischemic to ischemic type were also excluded from the study.

All patients underwent an extensive ophthalmic examination, including best corrected visual acuity (VA) on the Snellen's chart, intraocular pressure (IOP) measurement by applanation tonometry, slit-lamp and dilated examination. OCT was done on Stratus OCT and Fluorescein angiogram on Heidelberg retinal angiography if required. All patients underwent similar examinations on follow-up.

All patients were injected 0.5 mg in 0.05 ml of intravitreal Ranibizumab under complete aseptic precautions in the operation theatre following the standard protocol.

RESULTS:

Total of 61 eyes of 60 patients were examined. There were 36 males and 24 females. Average age was 55.23 years (ranging from 28 to 85 years). Right eye was affected in 33 patients and left eye was affected in 26 patients. There was a patient with bilateral affection.

The average period of presentation was 14.6 days (presenting from first day of symptom of upto 30 days).

24 patients had systemic hypertension, 4 had diabetes and 10 had both hypertension and diabetes. There was a patient presenting with cardiovascular pathology and a patient of hyperthyroidism. 20 patients had no systemic disease.

56 eyes were phakic and 5 were pseudophakic. The average IOP was 16 mm Hg. (ranging from 7 to 24)

The pretreatment type of macular edema on OCT was as:

- | | |
|-----------------------------|----------|
| 1. Cystoid edema (n = 18) | (Fig. 1) |
| 2. Subfoveal fluid (n = 14) | (Fig. 2) |
| 3. Mixed (n = 14) | |
| 4. Indeterminant (n= 15) | |

Table 1:

The patients with CME improved with an average of 2 lines or more on the Snellen's visual acuity chart while those presenting with SRF remained stable within a line of initial presentation. (*The $p = 0.006$ for CME as compared to $p = 0.038$ for SRF*)

The pretreatment OCT features of HRB were as:

- | | |
|----------------------|----------|
| 1. Good HRB (n = 35) | (Fig. 3) |
| 2. Poor HRB (n = 26) | (Fig. 4) |

Table 2:

(The $p = 0.0$ for high HRB than that of $p = 0.007$ for poor HRB, a high probability factor)

The average central macular thickness on pre-treatment OCT was 373 microns. On treatment the mean central macular thickness was 215.5 microns. But the central macular thickness did not have any bearing on the final visual acuity.

DISCUSSION:

Most retinal venous occlusions (RVO) occur at the lamina cribrosa or at arterio-venous crossing, leading to turbulent blood flow, endothelial damage and thrombus formation (Green et al 1981). Increased

central venous and intracapillary pressure results in the disruption of the blood retinal barrier, leading to retinal and macular edema (Gass 1997).

OCT can detect with precision the presence of CME and SRF, which would be underestimated with clinical or angiographic examination.

The pathology of SRF in venous occlusion is not well understood. It is believed that serous detachment may be related to the acute blockage of the entire central retinal venous system that results in acute leakage diffusely throughout the retinal capillaries, leading to edema of the retinal tissue and leakage into the subretinal space, which is not absorbed by the RPE. Major areas of venous occlusion may be associated with a greater degree of ischemia, which may leave less amount of healthy retina underlying the RPE to absorb the intraretinal and subretinal fluid

OCT allows us to evaluate the status of the third high reflectance band, which has been reported to show reflection derived from the RPE-photoreceptor complex

Integrity of the foveal retinal photoreceptor layer is associated with good visual acuity, while incomplete visualization of the third HRB in the fovea could suggest deterioration or disorganisation of photoreceptor cells. The reasons why the final status of the third HRB varies from case to case remain unclear. It is possible that more severe ischemia in the foveal photoreceptor cells during the acute or chronic phase of RVO might lead to significant photoreceptor cell death, resulting in the lack of the third HRB. It is also possible that more severe swelling in the foveal photoreceptor layer during the acute phase of RVO might result in significant disarrangement of photoreceptor cells even after resolution of the macular edema. In such a disarranged photoreceptor layer, the third HRB might not be detected as a reflective line.

The photoreceptor layer is swollen due to leakage from the affected capillaries, so the improper alignment of inner/outer segments could not be detected as a reflective line. In such cases, the foveal photoreceptor layer might be affected severely at the initial visit, resulting in an incomplete third HRB even after resolution of macular edema and poor visual outcome.

The current study showed that resolution of macular edema leads in many cases to significant improvement in visual acuity. However, when the third HRB in the parafoveal region is incomplete at the initial visit, visual recovery, even after successful treatment of the macular edema, could still be limited.

CONCLUSION:

OCT can guide to the prognostic outcome of patients to be treated with intravitreal ranibizumab for macular edema secondary to non-ischemic central retinal vein occlusion.

Declarations

‘Clinical trial number: not applicable.’

No Funding

Clinical trial number: not applicable.'

Declaration:

1. Ethics statement: The protocol was approved by in accordance with the Hamad Medical Corporation, Doha, Qatar with ID number MRC-01-25-1334 and passed the Research Governance Review Stage.
2. "Informed consent was obtained from all the individual participants for publication"
3. Informed consent was obtained from all the individual participants for participation in this study".
4. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The protocol was approved by Hamad Medical Corporation in accordance with the Quality Review. By the ID number MRC -01-25-1334.

(A copy of the approval is attached)

The study was conducted following the ethics committee approval following the guidelines of the Hamad Medical Corporation. Hence the MRC ID was issued.

Ethical Approval and accordance

The protocol was approved by the ethics committee of Hamad Medical Corporation in accordance with the guidelines and regulations of Declaration of Helsinki.

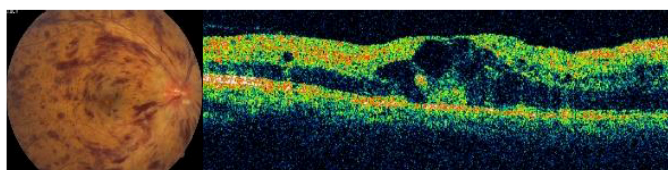
Tables

Tables 1 -2 are available in the Supplementary Files section.

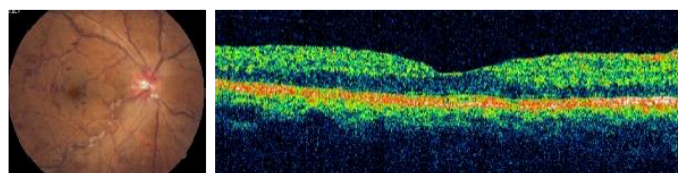
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6. Retina. June 2003 Volume 23, number 3.

Figures



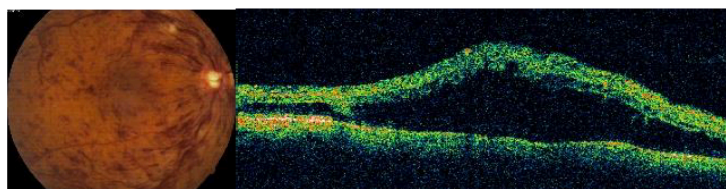
VA – 6/24 Pre Ranibizumab
OCT – CME pattern



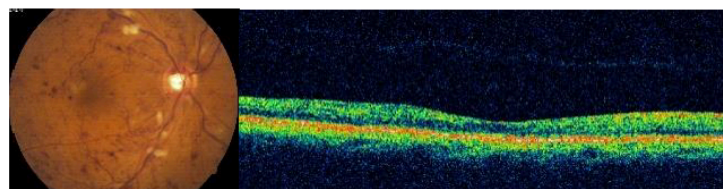
VA. - 6/6p Post Ranibizumab 1 month
Resolution of edema with return of
normal foveal contour

Figure 1

Patent with cystoid macular edema and after treatment



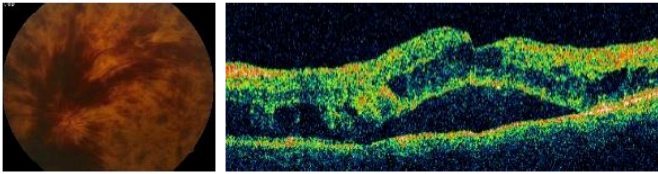
VA – 6/60 pre Ranibizumab
SRF presentation on OCT



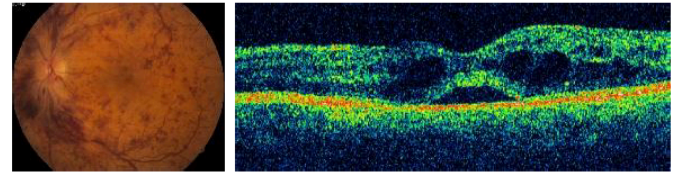
VA – 6/60 post Ranibizumab 1 month
Resolution of edema with normalization of
foveal contour.

Figure 2

Patent with sub retinal fluid and after treatment



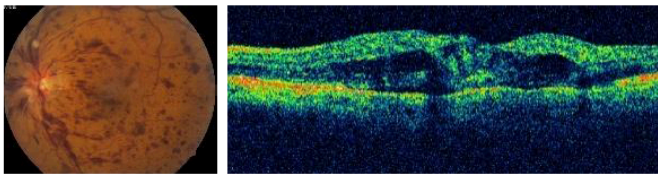
VA. – 6/60 Pre Ranibizumab
OCT – Good HRB



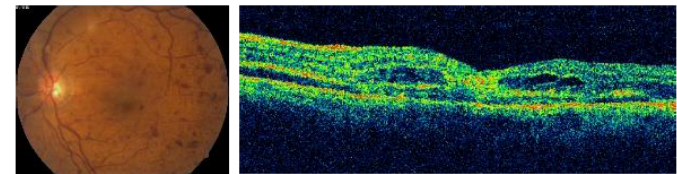
VA. – 6/24, 2 months Post Ranibizumab
Persistent edema, but good reflectivity

Figure 3

Patent with good high reflective band and after treatment



VA. - 6/60 pre Ranibizumab
OCT – poor reflectivity from HRB



VA – 6/36p 1 month post Ranibizumab
OCT – macular edema reduced

Figure 4

Patent with poor reflective band and after treatment

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Tables.docx](#)