

Original Article

# Comparative Analysis of Optical Coherence Tomography Angiography vs. Fluorescein Angiography in Diagnosing Retinal Vein Occlusion

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## ABSTRACT

**Background:** Retinal vein occlusion is a common retinal vascular disorder that may cause macular edema, retinal ischemia, neovascularization, and visual impairment. Fluorescein angiography has traditionally been used to evaluate retinal leakage and perfusion, while optical coherence tomography angiography provides non-invasive, depth-resolved assessment of retinal microvasculature. **Objective:** To compare the diagnostic findings of fluorescein angiography and optical coherence tomography angiography in patients with retinal vein occlusion. **Methods:** This cross-sectional diagnostic comparison study included 100 patients clinically diagnosed with branch or central retinal vein occlusion at a tertiary care hospital in Pakistan from January to June 2025. Each participant underwent ophthalmic examination, fluorescein angiography, and optical coherence tomography angiography. Imaging findings were summarized using frequencies, percentages, and 95% confidence intervals. **Results:** The mean age was  $58.40 \pm 11.20$  years, and branch retinal vein occlusion was present in 65.0% of patients. Fluorescein angiography detected capillary non-perfusion in 72.0%, vascular leakage in 66.0%, macular ischemia in 58.0%, and neovascularization in 19.0%. Optical coherence tomography angiography identified reduced vessel density in 76.0%, capillary dropout in 69.0%, enlarged foveal avascular zone in 63.0%, and microvascular abnormalities in 55.0%. **Conclusion:** Fluorescein angiography and optical coherence tomography angiography provided complementary diagnostic information. FA remained most useful for leakage assessment, while OCTA added non-invasive microvascular and vessel-density evaluation. **Keywords:** Retinal vein occlusion, Optical coherence tomography angiography, Fluorescein angiography, Macular ischemia, Capillary non-perfusion, Foveal avascular zone

## INTRODUCTION

Retinal vein occlusion (RVO) is a major retinal vascular disorder and remains one of the leading causes of retinal ischemia, macular edema, and vision loss worldwide. It is generally recognized as the second most common retinal vascular disease after diabetic retinopathy and is strongly associated with advancing age, systemic hypertension, diabetes mellitus, dyslipidemia, and other vascular risk factors (1,2). RVO develops when venous outflow from the retina is impaired, resulting in increased intraluminal venous pressure, retinal hemorrhage, capillary non-perfusion, vascular leakage, and ischemic macular injury. The clinical consequences vary according to the site and extent of obstruction, with branch retinal vein occlusion (BRVO) typically affecting a sector of the retina and central retinal vein occlusion (CRVO) involving more widespread retinal circulation compromise (2,10,11). Because

visual prognosis depends substantially on the severity of ischemia, macular edema, and neovascular risk, accurate imaging-based evaluation is central to diagnosis, classification, treatment planning, and follow-up.

Fluorescein angiography (FA) has historically served as the conventional clinical reference modality for evaluating retinal vascular disorders. By using intravenously administered fluorescein dye and sequential fundus photography, FA allows direct visualization of dye transit through the retinal circulation and provides clinically important information regarding capillary non-perfusion, vascular leakage, macular ischemia, and neovascularization (5,6). These features are particularly relevant in RVO because leakage contributes to macular edema, while non-perfusion reflects ischemic retinal injury and may indicate increased risk of neovascular complications (9,15). FA therefore remains highly useful when clinicians need to assess vascular leakage and peripheral perfusion abnormalities for treatment decisions such as anti-vascular endothelial growth factor therapy, laser photocoagulation, or closer ischemic monitoring.

Despite its clinical value, FA has important limitations. It is invasive, requires venous access and dye administration, and may cause nausea, vomiting, urticaria, allergic reactions, or rarely severe hypersensitivity reactions (6,17). FA also provides a largely two-dimensional representation of retinal circulation and does not reliably separate the superficial and deep retinal capillary plexuses. This limitation may reduce its ability to characterize layer-specific microvascular damage, particularly in macular ischemia and capillary remodeling (5,7). In addition, repeated FA may not be feasible or desirable for all patients, especially those requiring frequent monitoring over the course of chronic retinal vascular disease.

Optical coherence tomography angiography (OCTA) has emerged as a non-invasive imaging technique that detects motion contrast generated by erythrocyte movement within retinal and choroidal vessels. Unlike FA, OCTA does not require injectable dye and can provide depth-resolved visualization of the superficial capillary plexus, deep capillary plexus, outer retinal flow signals, and choriocapillaris depending on device capability and segmentation protocol (3,4,7). In RVO, OCTA can demonstrate reduced vessel density, capillary dropout, disruption of the foveal avascular zone (FAZ), collateral vessel formation, and microvascular rarefaction (4,13,14,19). Quantitative parameters such as vessel density and FAZ area may also provide objective markers of macular ischemia and may be useful for monitoring disease progression and treatment response (13,14,21).

The major diagnostic advantage of OCTA lies in its ability to visualize retinal microvasculature in a layer-specific and repeatable manner. Several studies have shown that OCTA can identify capillary non-perfusion and FAZ enlargement in RVO and may correlate with visual function and ischemic severity (3,4,19,21). However, OCTA has limitations that prevent it from fully replacing FA in all clinical settings. Because OCTA detects flow rather than dye leakage, it cannot directly demonstrate vascular leakage, which remains an essential feature in assessing macular edema and blood-retinal barrier disruption (6,7). OCTA is also susceptible to motion artifacts, projection artifacts, segmentation errors, and reduced image quality in eyes with poor fixation, media opacity, dense hemorrhage, or severe retinal edema (8,12). Furthermore, standard OCTA scans may have a smaller field of view than ultra-widefield FA, potentially limiting detection of peripheral ischemia (2).

The comparative clinical role of OCTA and FA in RVO therefore remains important, particularly in settings where clinicians must balance diagnostic yield, patient safety, availability of equipment, and need for repeated imaging. Existing literature suggests that OCTA and FA provide overlapping but non-identical diagnostic information: FA remains stronger for leakage and widefield perfusion assessment, whereas OCTA is stronger for non-invasive, quantitative, layer-specific assessment of retinal microvascular architecture (2,3,5,7). However, local evidence from Pakistan remains limited, despite the increasing availability of advanced retinal imaging systems in tertiary ophthalmology centers and the growing burden of vascular retinal disease in aging populations.

The present study was designed to compare OCTA and FA in patients clinically diagnosed with RVO at a tertiary care hospital in Pakistan. The population of interest comprised adults with BRVO or CRVO, the index imaging modality was OCTA, the comparator modality was FA, and the diagnostic outcomes included detection of capillary non-perfusion, vascular leakage, macular ischemia, reduced vessel density, FAZ enlargement, capillary dropout, and other microvascular abnormalities. The objective was to evaluate the complementary diagnostic contribution of OCTA relative to FA in identifying clinically relevant retinal vascular changes in RVO, with particular attention to features where each modality is expected to perform differently.

## MATERIALS AND METHODS

This diagnostic comparison study was conducted in the retina clinic and ophthalmology diagnostic unit of a tertiary care hospital in Pakistan to compare optical coherence tomography angiography (OCTA) with fluorescein angiography (FA) in patients diagnosed with retinal vein occlusion (RVO). The study followed a cross-sectional observational design in which both imaging modalities were performed in the same participants during the same clinical visit or within a short interval to minimize temporal variation in retinal vascular findings. The index test was OCTA, while FA was used as the conventional clinical comparator for evaluating leakage, perfusion defects, and macular ischemic changes. Because OCTA and FA measure different vascular phenomena, the study was designed to assess comparative and complementary diagnostic findings rather than to claim complete interchangeability between the two modalities.

The study was conducted over six months, from January 2025 to June 2025. Eligible participants were adults aged 18 years or older who were clinically diagnosed with RVO by an ophthalmologist and were able to undergo both OCTA and FA imaging. Both central retinal vein occlusion and branch retinal vein occlusion were included. Patients were excluded if they had coexisting retinal disease likely to confound image interpretation, including diabetic retinopathy, age-related macular degeneration, retinal detachment, previous retinal surgery, dense cataract, vitreous hemorrhage, poor-quality retinal images, known fluorescein dye allergy, or inability to cooperate during imaging. Consecutive eligible patients attending the retina clinic during the study period were invited to participate, and one eye per patient was included in the analysis to avoid duplication of observations. When both eyes were affected, the eye with clearer imaging quality and more clinically active RVO findings was selected.

After ethical approval and written informed consent, demographic and clinical data were collected using a structured clinical form. Recorded variables included age, sex, relevant systemic history, presence of hypertension or diabetes, duration of visual symptoms, type of RVO, and clinical examination findings. Each participant underwent best-corrected visual acuity assessment, slit-lamp anterior segment examination, intraocular pressure measurement, and dilated fundus examination before retinal imaging. The primary diagnostic features evaluated across imaging modalities were capillary non-perfusion and macular ischemia. Secondary imaging features included vascular leakage, retinal hemorrhage, neovascularization, reduced vessel density, capillary dropout, enlargement of the foveal avascular zone, and retinal microvascular abnormalities.

FA was performed using a digital fundus camera system after pharmacological pupillary dilation. A 5 ml fluorescein dye injection was administered intravenously through a peripheral vein, and sequential retinal images were obtained during dye circulation. FA images were assessed for capillary non-perfusion, vascular leakage, macular ischemia, retinal hemorrhage, and neovascularization. OCTA was performed using a spectral-domain optical coherence tomography system equipped with angiography software. OCTA scanning was performed without dye injection while the patient fixated on the internal target. Images were evaluated for vessel density reduction in the superficial and deep capillary plexuses, capillary dropout, FAZ enlargement, and microvascular abnormalities. Images with motion artifact,

segmentation failure, signal loss, or poor media clarity sufficient to impair interpretation were excluded from image-level analysis.

To reduce measurement and interpretation bias, FA and OCTA images were reviewed independently by two experienced retinal specialists. Reviewers assessed each imaging modality separately and were blinded to the other reviewer's interpretation. Disagreements were resolved by consensus. The analysis specifically compared the ability of each modality to identify clinically relevant RVO-related vascular abnormalities, while recognizing that leakage is directly assessable by FA but not by OCTA. Inter-observer agreement was planned using Cohen's kappa for categorical imaging findings where paired reader assessments were available.

Data were entered and analyzed using IBM SPSS Statistics version 26. Continuous variables were summarized as mean and standard deviation, while categorical variables were summarized as frequencies and percentages. Detection rates of key imaging findings were compared between FA and OCTA using chi-square or McNemar testing where paired binary comparisons were appropriate. Agreement between modalities for shared diagnostic features, including capillary non-perfusion and macular ischemia, was planned using kappa statistics with 95% confidence intervals. Where a conventional reference classification was required for diagnostic comparison, FA findings were treated as the clinical comparator for leakage and perfusion-related abnormalities, while OCTA-derived microvascular parameters were interpreted as complementary structural-flow findings rather than direct substitutes for dye leakage. Statistical significance was set at  $\alpha = 0.05$ , and all confidence intervals were calculated at the 95% level.

Potential sources of bias were addressed through consecutive sampling, standardized eligibility criteria, same-patient imaging with both modalities, independent image interpretation, and exclusion of poor-quality scans. Confounding by coexisting retinal pathology was minimized through exclusion criteria. Data integrity was maintained through structured data collection, single-eye inclusion per participant, verification of imaging findings by retinal specialists, and removal of personal identifiers before analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki, and all participants provided written informed consent before enrollment.

## RESULTS

A total of 100 patients clinically diagnosed with retinal vein occlusion were included. All participants underwent both fluorescein angiography and optical coherence tomography angiography. The mean age was  $58.40 \pm 11.20$  years. Male patients comprised 56.0% of the sample, while female patients comprised 44.0%. Branch retinal vein occlusion was more frequent than central retinal vein occlusion, accounting for 65.0% and 35.0% of cases, respectively.

*Table 1. Baseline demographic and clinical characteristics of study participants*

Variable	Frequency / Mean	Percentage / SD
Total participants	100	100.0%
Age, years	58.40	11.20
Male	56	56.0%
Female	44	44.0%
Age 30–40 years	8	8.0%
Age 41–50 years	21	21.0%
Age 51–60 years	34	34.0%
Age 61–70 years	25	25.0%
Age >70 years	12	12.0%
Branch retinal vein occlusion	65	65.0%
Central retinal vein occlusion	35	35.0%

Fluorescein angiography identified capillary non-perfusion in 72.0% of patients, vascular leakage in 66.0%, retinal hemorrhage in 61.0%, macular ischemia in 58.0%, and neovascularization in 19.0%.

Capillary non-perfusion was the most common FA finding, while neovascularization was the least frequent finding.

**Table 2. Diagnostic findings observed on fluorescein angiography**

FA finding	n/N	Percentage	95% CI
Capillary non-perfusion	72/100	72.0%	62.5–80.1%
Vascular leakage	66/100	66.0%	56.3–74.5%
Retinal hemorrhage	61/100	61.0%	51.2–70.0%
Macular ischemia	58/100	58.0%	48.2–67.2%
Neovascularization	19/100	19.0%	12.5–27.8%

Optical coherence tomography angiography demonstrated reduced vessel density in 76.0% of patients, capillary dropout in 69.0%, enlarged foveal avascular zone in 63.0%, and other microvascular abnormalities in 55.0%. Reduced vessel density was the most frequent OCTA abnormality.

**Table 3. Diagnostic findings observed on optical coherence tomography angiography**

OCTA finding	n/N	Percentage	95% CI
Reduced vessel density	76/100	76.0%	66.7–83.3%
Capillary dropout	69/100	69.0%	59.4–77.2%
Enlarged foveal avascular zone	63/100	63.0%	53.2–71.8%
Microvascular abnormalities	55/100	55.0%	45.3–64.4%

Both modalities detected clinically important vascular abnormalities, but their diagnostic strengths differed. FA uniquely demonstrated vascular leakage, while OCTA uniquely quantified vessel density and provided layer-specific microvascular information. Because the available dataset provides only aggregate counts rather than paired patient-level cross-tabulations, sensitivity, specificity, positive predictive value, negative predictive value, McNemar p-values, Cohen's kappa, and paired effect estimates could not be calculated validly from the current data.

**Table 4. Comparative diagnostic capability of FA and OCTA based on available study data**

Diagnostic feature	FA finding	OCTA finding
Capillary non-perfusion / dropout	72.0%	69.0%
Vascular leakage	66.0%	Not directly measurable
Macular ischemia / FAZ enlargement	58.0%	63.0%
Vessel density measurement	Not available	76.0% reduced vessel density
Microvascular abnormalities	Moderate qualitative assessment	55.0% detected
Layer-specific vascular imaging	Not available	Available

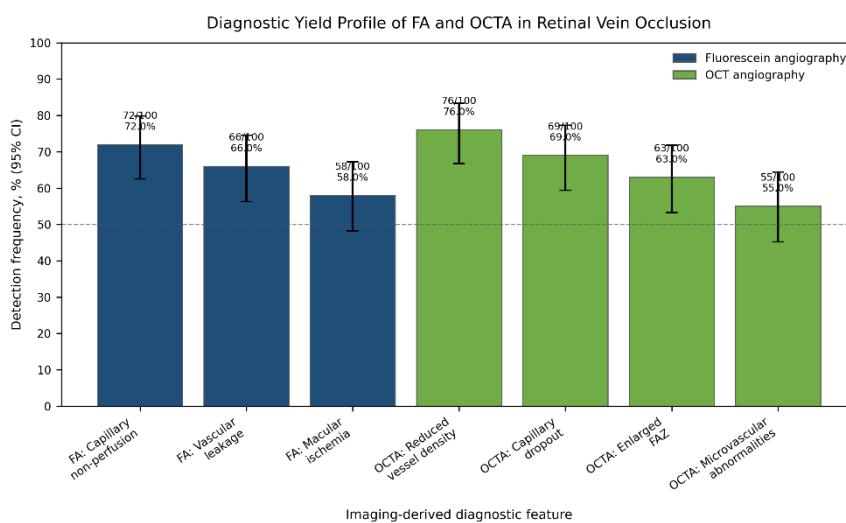
The study included 100 patients with clinically diagnosed retinal vein occlusion, with complete imaging data available for both fluorescein angiography and optical coherence tomography angiography. The sample predominantly represented older adults, with a mean age of 58.40 years and the largest age group falling between 51 and 60 years. Male patients were slightly more frequent than female patients. Branch retinal vein occlusion was the dominant clinical subtype, affecting nearly two-thirds of the sample, whereas central retinal vein occlusion accounted for just over one-third of cases, as shown in Table 1.

Fluorescein angiography demonstrated a high frequency of vascular abnormalities related to ischemia and leakage. Capillary non-perfusion was identified in 72.0% of patients, making it the most common FA finding. Vascular leakage was also frequent, affecting 66.0% of patients, supporting the continued clinical value of FA for assessing blood–retinal barrier disruption. Macular ischemia was detected in 58.0%, while neovascularization was identified in 19.0%, indicating that a smaller but clinically important subset of patients showed advanced ischemic complications, as shown in Table 2.

Optical coherence tomography angiography provided additional microvascular information that was not directly available through FA. Reduced vessel density was observed in 76.0% of patients, representing the most common OCTA abnormality. Capillary dropout was detected in 69.0%, while enlargement of the foveal avascular zone was present in 63.0%. These findings indicate that OCTA was particularly useful for identifying flow-based microvascular compromise and macular capillary disruption, as shown in Table 3.

The comparative pattern showed that FA and OCTA provided complementary rather than identical diagnostic information. FA remained superior for vascular leakage because dye extravasation is directly visible on angiography but cannot be directly measured by OCTA. Conversely, OCTA provided clinically relevant structural-flow information, including reduced vessel density, capillary dropout, FAZ enlargement, and layer-specific retinal vascular assessment. On aggregate comparison, ischemic capillary abnormalities were frequent on both modalities, with FA showing capillary non-perfusion in 72.0% and OCTA showing capillary dropout in 69.0%, as shown in Table 4.

Because only aggregate counts were available, valid paired inferential testing could not be performed. Diagnostic accuracy statistics such as sensitivity, specificity, predictive values, likelihood ratios, McNemar p-values, and kappa agreement require patient-level paired results showing whether the same individuals were positive or negative on both modalities. Therefore, the present results support a descriptive comparative interpretation: FA was most informative for leakage and perfusion assessment, while OCTA added non-invasive, quantitative, and layer-specific evaluation of retinal microvascular damage.



**Figure 1 Diagnostic Yield Profile Of FA And OCTA In Retinal Vein Occlusion**

Diagnostic-yield profile of fluorescein angiography and optical coherence tomography angiography in 100 patients with retinal vein occlusion. OCTA most frequently identified reduced vessel density in 76.0% of patients, followed by capillary dropout in 69.0% and enlarged foveal avascular zone in 63.0%, while FA most frequently demonstrated capillary non-perfusion in 72.0% and vascular leakage in 66.0%. The pattern supports complementary diagnostic utility, with FA providing superior leakage assessment and OCTA contributing non-invasive microvascular and perfusion-density information.

## DISCUSSION

The present study compared fluorescein angiography and optical coherence tomography angiography in 100 patients with retinal vein occlusion and demonstrated that both modalities identified clinically meaningful vascular abnormalities, but with different diagnostic strengths. Fluorescein angiography most frequently demonstrated capillary non-perfusion in 72.0% of patients, followed by vascular leakage in 66.0%, retinal hemorrhage in 61.0%, macular ischemia in 58.0%, and neovascularization in 19.0%. OCTA most frequently identified reduced vessel density in 76.0%, followed by capillary dropout in 69.0%, enlarged foveal avascular zone in 63.0%, and microvascular abnormalities in 55.0%. These findings indicate that FA remains particularly useful for identifying leakage and perfusion abnormalities, whereas OCTA provides additional non-invasive information regarding capillary architecture, vessel density, and macular microvascular compromise. Because patient-level paired cross-tabulated data were not available, sensitivity, specificity, predictive values, likelihood ratios, McNemar

testing, and agreement statistics could not be calculated; therefore, the findings should be interpreted as descriptive evidence of complementary diagnostic utility rather than definitive diagnostic superiority.

The observed diagnostic pattern is consistent with previous literature showing that FA and OCTA assess related but distinct vascular phenomena in retinal vascular disease. FA remains valuable because fluorescein leakage directly reflects blood–retinal barrier disruption, which is a key mechanism underlying macular edema in RVO (5,6). Earlier studies have also emphasized the role of FA in detecting capillary non-perfusion, macular ischemia, and neovascular changes, particularly where peripheral retinal ischemia is clinically relevant (2,15). Conversely, OCTA has been reported to provide high-resolution, depth-resolved visualization of superficial and deep capillary plexuses, allowing detection of vessel density reduction, capillary dropout, and FAZ enlargement (3,4,7,19). The present study aligns with this evidence by showing high OCTA detection frequencies for reduced vessel density and capillary dropout. However, unlike studies with paired image-level diagnostic matrices, the present dataset did not permit formal agreement testing or diagnostic accuracy estimation against a reference standard, limiting direct comparison with accuracy-focused reports.

The biological and clinical basis for these findings is plausible. RVO causes venous obstruction, increased hydrostatic pressure, hemorrhage, endothelial dysfunction, and capillary non-perfusion. FA captures dye leakage and non-perfusion patterns because fluorescein extravasation reflects vascular barrier breakdown, while absence or delay of dye filling reflects perfusion defects. OCTA, in contrast, detects motion contrast from flowing erythrocytes and is therefore better suited to identifying microvascular flow reduction, capillary rarefaction, FAZ irregularity, and layer-specific vascular compromise. This explains why OCTA detected reduced vessel density in a high proportion of patients, while FA remained uniquely informative for leakage. The inability of OCTA to directly visualize leakage is not a methodological weakness of the present study but a known modality-specific limitation, because OCTA is flow-based rather than dye-diffusion-based (7,8).

This study has several strengths. All patients underwent both imaging modalities, allowing assessment of the same clinical population using two commonly applied retinal vascular imaging techniques. Consecutive sampling reduced selective recruitment, and image interpretation by retinal specialists strengthened clinical validity. The study also addressed a relevant evidence gap by providing local data from a tertiary care setting in Pakistan, where OCTA availability is increasing but comparative evidence remains limited. Nevertheless, important limitations should be acknowledged. The study was single-center and included a modest sample size. The available results were aggregate rather than patient-level paired data, preventing calculation of sensitivity, specificity, kappa agreement, confidence intervals for paired differences, or adjusted analyses. The study also lacked subgroup analysis by BRVO and CRVO, did not incorporate visual acuity correlations, and did not evaluate longitudinal treatment response. Potential confounding by systemic vascular factors such as hypertension and diabetes was not analytically controlled, although major coexisting retinal diseases were excluded.

Clinically, these findings support the use of FA and OCTA as complementary modalities in RVO evaluation. FA should remain important when leakage, macular edema-related vascular disruption, neovascularization, or peripheral perfusion status must be assessed. OCTA may be particularly useful for repeated follow-up because it is non-invasive and provides quantitative or semi-quantitative information about vessel density, capillary dropout, and FAZ changes. Future studies should use patient-level paired diagnostic matrices, predefined reference standards, standardized OCTA scan protocols, inter-observer agreement analysis, and subgroup analysis by RVO subtype. Larger multicenter studies should also examine whether OCTA parameters such as vessel density and FAZ area predict visual acuity, macular edema recurrence, ischemic progression, or treatment response.

## CONCLUSION

In this diagnostic comparison study of patients with retinal vein occlusion, fluorescein angiography and optical coherence tomography angiography demonstrated complementary clinical value. FA was most useful for identifying vascular leakage, capillary non-perfusion, macular ischemia, and neovascularization, whereas OCTA provided non-invasive visualization of reduced vessel density, capillary dropout, FAZ enlargement, and microvascular abnormalities. These findings support OCTA as a valuable adjunct rather than a complete replacement for FA. Future multicenter studies using paired patient-level data, standardized reference criteria, diagnostic accuracy measures, and visual outcome correlations are required to define the precise role of OCTA in routine RVO assessment and follow-up.

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