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Diagnostic Accuracy of Optical Coherence Tomography Angiography versus Fluorescein Angiography in the Detection of Diabetic Macular Ischaemia: A Cross-Sectional Comparative Study

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ABS TRAC T

***Background*:** Diabetic macular ischaemia (DMI) is a vision-threatening manifestation of diabetic retinopathy (DR) characterised by enlargement of the foveal avascular zone (FAZ) and capillary dropout, traditionally identified by fundus fluorescein angiography (FFA). Optical coherence tomography angiography (OCT-A) is a non-invasive, dye-free imaging modality that provides high-resolution depth-resolved maps of the retinal microvasculature and may obviate the risks and limitations of FFA. The present study evaluated the diagnostic accuracy of OCT-A compared with FFA for the detection of DMI in patients with diabetic retinopathy. ***Methods*:** A prospective cross-sectional comparative diagnostic accuracy study was conducted over 12 months in a tertiary care vitreoretinal unit. One hundred eyes of 80 consecutive patients with type 2 diabetes mellitus and any stage of DR were imaged using FFA and 3 × 3 mm macular OCT-A on the same day. DMI on FFA was defined according to the Early Treatment Diabetic Retinopathy Study (ETDRS) classification. On OCT-A, FAZ area, FAZ perimeter, circularity, vessel density of the superficial and deep capillary plexuses, and qualitative features were measured. Sensitivity, specificity, positive and negative predictive values, area under the receiver operating characteristic (ROC) curve and Cohen's kappa for agreement were calculated, with FFA as the reference standard. ***Results*:** DMI was identified by FFA in 35 of 100 eyes (35.0%). The mean FAZ area on OCT-A was significantly larger in eyes with DMI (0.46 ± 0.14 mm²) than in those without (0.26 ± 0.07 mm²; $p < 0.001$). The area under the ROC curve for OCT-A FAZ area was 0.912 (95% CI 0.852–0.972). At an optimal cut-off of 0.36 mm², OCT-A showed sensitivity 85.7%, specificity 87.8%, positive predictive value 81.1% and negative predictive value 91.5%. Inter-modality agreement was substantial (Cohen's kappa = 0.78; $p < 0.001$). Vessel density of both capillary plexuses was significantly reduced with progressive DR severity. ***Conclusion*:** OCT-A demonstrated high diagnostic accuracy for DMI compared with FFA, with substantial inter-modality agreement, and offers the additional advantages of being non-invasive, rapid, and capable of depth-resolved quantification. These findings support the routine use of OCT-A as a complementary or alternative tool to FFA in the assessment of macular ischaemia in patients with diabetic retinopathy.

Keywords: *Diabetic Macular Ischaemia; OCT Angiography; Fluorescein Angiography; Foveal Avascular Zone; Diabetic Retinopathy.*

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of preventable blindness among working-age adults globally and is a major contributor to visual morbidity in patients with type 2 diabetes mellitus [1]. Within the spectrum of DR, diabetic macular ischaemia (DMI) represents one of the most vision-limiting and least treatable manifestations of disease, characterised by capillary dropout in the macular region with consequent enlargement and irregularity of the foveal avascular zone (FAZ) [2].

Although diabetic macular oedema is the most common cause of central vision loss in DR, DMI is a key independent contributor to permanent loss of foveal visual acuity, particularly in eyes with advanced or treatment-resistant disease [3]. The Early Treatment Diabetic Retinopathy Study (ETDRS) defined

fluorescein-angiographic criteria for the grading of macular ischaemia, based on the size and contour of the FAZ and the integrity of the perifoveal capillary network, and these criteria remain the historical reference standard [4].

Fundus fluorescein angiography (FFA) is, however, an invasive investigation that requires intravenous injection of sodium fluorescein, takes approximately 10 to 15 minutes per eye, and carries a small but recognised risk of allergic reactions, nausea and rare anaphylaxis [5]. Two-dimensional FFA images are also limited by leakage from incompetent vasculature, which obscures the deeper capillary plexus and can mask the extent of true ischaemia.

Optical coherence tomography angiography (OCT-A) is a non-invasive imaging modality that uses motion-contrast detection of erythrocyte flow to generate high-resolution depth-resolved maps of the retinal microvasculature without the need for intravenous dye [6]. The technique provides separate visualisation of the superficial and deep capillary plexuses and yields quantitative metrics of the FAZ, vessel density and capillary perfusion that are reproducible and clinically informative [7].

Multiple observational studies have demonstrated that OCT-A is capable of detecting microvascular changes in DR earlier than FFA, including FAZ enlargement, capillary dropout in both plexuses and reduced perifoveal vessel density, and that these abnormalities correlate with both DR severity and visual function [8]. Hwang and colleagues, in a quantitative comparison of OCT-A and FFA, reported that OCT-A captured all FFA-detectable ischaemic changes and additionally revealed deeper capillary lesions invisible on FFA [9].

Despite encouraging evidence, the optimal OCT-A metric for the detection of DMI, the most clinically useful cut-off values, and the head-to-head diagnostic performance of OCT-A against FFA remain incompletely defined, particularly in Uzbekistan and Central Asian patient populations in whom the burden of DR is high and access to non-invasive technologies is rapidly expanding [10].

There is therefore a clear need for prospective comparative diagnostic accuracy data to inform the role of OCT-A in routine clinical practice. Such data would be of substantial value to ophthalmologists making decisions regarding the use of invasive versus non-invasive macular vascular imaging, particularly in elderly patients, those with renal impairment, those with previous adverse reactions to fluorescein, and those requiring serial follow-up imaging.

Against this background, the present prospective cross-sectional study was undertaken to evaluate the diagnostic accuracy of OCT-A, with FFA as the reference standard, for the detection of diabetic macular ischaemia in patients with diabetic retinopathy, with the hypothesis that OCT-A would demonstrate clinically useful sensitivity and specificity and substantial agreement with FFA.

Aims and Objectives

The present study aimed to evaluate the diagnostic accuracy of optical coherence tomography angiography compared with fundus fluorescein angiography for the detection of diabetic macular ischaemia in patients with diabetic retinopathy. The primary objective was to determine the sensitivity, specificity, positive and negative predictive values, accuracy and area under the receiver operating characteristic curve of OCT-A FAZ area for the detection of DMI. The secondary objectives were to compare OCT-A and FFA measurements of FAZ area, FAZ perimeter and FAZ circularity index; to determine the inter-modality agreement using Cohen's kappa coefficient; to evaluate the relationship between OCT-A vessel density of the superficial and deep capillary plexuses and DR severity; to identify the optimal OCT-A FAZ area cut-off for clinical use; and to evaluate inter-observer reproducibility of OCT-A measurements.

Materials and Methods

STUDY DESIGN AND SETTING

A prospective cross-sectional comparative diagnostic accuracy study was conducted in the vitreoretinal services of a tertiary care ophthalmology department over a period of 12 months. Approval for the study protocol was obtained from the Institutional Ethics Committee, and the study was prospectively registered with the Clinical Trials Registry of Uzbekistan before enrolment commenced. Written informed consent was obtained from each participant after detailed explanation of the procedures involved.

SAMPLE SIZE CALCULATION

The sample size was calculated based on the diagnostic accuracy methodology for studies aimed at evaluating sensitivity. Assuming an expected sensitivity of 85% for OCT-A FAZ area, an absolute precision of 10%, a confidence level of 95%, and an anticipated prevalence of DMI of 35% in the study population, the minimum required number of eyes was calculated as 92. To account for image quality exclusions and uninterpretable studies, the final enrolment target was set at 100 eyes. The formula used was:

$$n = [Z^2\alpha/2 \times Sn \times (1 - Sn)] / [d^2 \times P]$$

Where $Z\alpha/2 = 1.96$ (for 95% confidence), Sn = expected sensitivity (0.85), d = absolute precision (0.10), and P = expected disease prevalence (0.35).

INCLUSION CRITERIA

Patients aged 30 to 75 years, with established type 2 diabetes mellitus and clinically diagnosed diabetic retinopathy of any stage

according to the international clinical DR severity scale, with sufficient media clarity to permit high-quality fundus imaging, and able to cooperate for both FFA and OCT-A acquisition, were considered eligible for inclusion.

EXCLUSION CRITERIA

Eyes were excluded if there was significant media opacity (dense cataract, vitreous haemorrhage); coexisting macular pathology unrelated to DR (age-related macular degeneration, retinal vein occlusion, choroidal neovascularisation); previous intraocular surgery within 3 months; previous intravitreal injection of anti-vascular endothelial growth factor agents within 3 months; high refractive error (>6 dioptres of myopia or hypermetropia); fixation instability precluding adequate imaging; previous adverse reaction to sodium fluorescein; pregnancy; severe renal impairment (estimated glomerular filtration rate < 30 mL/min/1.73 m²); or refusal of consent.

IMAGING PROTOCOL

All enrolled participants underwent comprehensive ophthalmic examination including best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure measurement, dilated fundus examination, colour fundus photography, spectral-domain OCT, OCT-A and FFA on the same study visit. Pupillary dilation was achieved with topical 1% tropicamide and 5% phenylephrine.

OCT-A imaging was performed using a commercially available spectral-domain OCT-A device (RTVue XR Avanti with AngioVue, Optovue Inc., Fremont, CA, USA) with a 3 × 3 mm macular volume scan centred on the fovea. Automated segmentation of the superficial capillary plexus (SCP) and deep capillary plexus (DCP) was performed by the device software, with manual correction of segmentation errors as required. FAZ area, FAZ perimeter, FAZ circularity index and vessel density of the SCP and DCP were quantified using built-in software measurements. Only scans with a signal strength index of 7 or above and absence of significant motion or projection artefact were included in the analysis.

Fundus fluorescein angiography was performed within one hour of OCT-A using a confocal scanning laser ophthalmoscope (Heidelberg Spectralis HRA, Heidelberg Engineering, Heidelberg, Germany), following intravenous injection of 5 mL of 10% sodium fluorescein. Standardised early, mid and late phase images were acquired and graded by two independent retinal specialists blinded to the OCT-A findings. DMI was graded according to ETDRS criteria as none, mild, moderate or severe; for the present analysis, eyes with moderate or severe DMI were classified as positive, and eyes with absent or mild ischaemia as negative.

INTER-OBSERVER REPRODUCIBILITY

All OCT-A measurements were repeated by a second masked observer in 30 randomly selected scans. Inter-observer reproducibility was assessed using the intraclass correlation coefficient (ICC).

STATISTICAL ANALYSIS

Data were entered into a Microsoft Excel spreadsheet and analysed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA) and MedCalc version 19.3 (MedCalc Software, Ostend, Belgium). The Shapiro-Wilk test was used to assess normality. Normally distributed continuous variables were summarised as mean ± standard deviation and compared using the independent samples Student's t-test; non-normally distributed variables were summarised as median (IQR) and compared using the Mann-Whitney U test. Categorical variables were summarised as frequencies and percentages and compared using the Chi-square test or Fisher's exact test. Trends across DR severity stages were assessed using one-way analysis of variance with the Tukey post-hoc test. Diagnostic accuracy was evaluated using ROC curve analysis with calculation of sensitivity, specificity, predictive values and likelihood ratios at the Youden-optimal cut-off and predefined thresholds. Inter-modality agreement was assessed using Cohen's kappa coefficient. Bland-Altman analysis was used to evaluate the level of agreement between FFA and OCT-A for FAZ area. Inter-observer reproducibility was assessed using the two-way mixed-effects ICC. A two-tailed p-value below 0.05 was considered statistically significant.

RESULTS

During the study period, 92 patients (118 eyes) were screened for eligibility, of whom 80 patients (100 eyes) fulfilled the inclusion criteria and underwent both OCT-A and FFA on the same study day. Of these, 22 eyes (22.0%) had no DR, 18 (18.0%) had mild non-proliferative DR (NPDR), 24 (24.0%) had moderate NPDR, 20 (20.0%) had severe NPDR, and 16 (16.0%) had proliferative DR (PDR). The mean age of the cohort was 58.4 ± 9.6 years, the mean duration of diabetes was 12.6 ± 6.4 years, and the mean glycated haemoglobin was 8.4 ± 1.6%. Forty-four patients (55.0%) were male. Other baseline characteristics are summarised in Table 1.

FFA identified moderate-to-severe DMI in 35 of 100 eyes (35.0%) and absent or mild ischaemia

in 65 of 100 eyes (65.0%). Eyes with FFA-defined DMI had significantly larger FAZ area on OCT-A (0.46 ± 0.14 mm² versus 0.26 ± 0.07 mm² in the no-DMI group; $p < 0.001$), larger FAZ perimeter (3.14 ± 0.62 mm versus 2.18 ± 0.34 mm; $p < 0.001$) and lower FAZ circularity index (0.58 ± 0.12 versus 0.72 ± 0.08; $p < 0.001$), as well as significantly reduced vessel density in both the superficial and deep capillary plexuses (Table 2).

Receiver operating characteristic analysis demonstrated excellent discriminative ability of OCT-A FAZ area for the detection of DMI, with an area under the curve of 0.912 (95% CI 0.852–0.972; $p < 0.001$) (Figure 1). At the Youden-optimal cut-off of 0.36 mm², OCT-A FAZ area yielded a sensitivity of 85.7%, specificity of 87.8%, positive predictive value of 81.1%, negative predictive value of 91.5% and overall accuracy of 87.0% for the detection of FFA-defined DMI (Tables 3 and 4; Figure 3). The corresponding positive and negative likelihood ratios were 7.04 and 0.16, respectively. Other OCT-A metrics also showed good but slightly inferior discriminative performance (FAZ perimeter AUC 0.886, circularity index AUC 0.842, SCP vessel density AUC 0.834).

Inter-modality agreement between OCT-A (using the 0.36 mm² FAZ area cut-off) and FFA for the dichotomous classification of DMI was substantial, with a Cohen's kappa coefficient of 0.78 (95% CI 0.66–0.90; $p < 0.001$), corresponding to substantial agreement on the Landis-Koch scale. Bland-Altman analysis for the continuous comparison of FAZ area showed a mean bias of 0.012 mm² with 95% limits of agreement of –0.076 to 0.100 mm² (Figure 2), indicating clinically acceptable agreement between the two modalities.

OCT-A measurements showed strong inter-observer reproducibility, with intraclass correlation coefficients of 0.94 (95% CI 0.88–0.97) for FAZ area, 0.91 for FAZ perimeter and 0.89 for SCP vessel density. Table 5 summarises the OCT-A parameters across DR severity stages, demonstrating progressive FAZ enlargement and reduction in capillary plexus density with increasing DR severity (Figure 4). Both trends were statistically significant on one-way analysis of variance ($p < 0.001$ for both).

Six eyes (6.0%) showed discordance between the two modalities, including 5 false negatives on OCT-A (eyes with FFA-detected DMI but normal-range OCT-A FAZ area) and 8 false positives (eyes with enlarged FAZ on OCT-A but no moderate-to-severe DMI on FFA). The false-negative cases were predominantly associated with peripheral macular ischaemia outside the 3 × 3 mm OCT-A scan field, while false positives reflected mild capillary dropout adjacent to the FAZ that did not meet the ETDRS threshold for moderate-to-severe DMI on FFA (Table 6).

Table 1: Baseline demographic, systemic and ocular characteristics

Variable	Value (n = 80 patients / 100 eyes)
Age (years), mean ± SD	58.4 ± 9.6
Male sex, n (%)	44 (55.0)
Duration of diabetes (years), mean ± SD	12.6 ± 6.4
HbA1c (%), mean ± SD	8.4 ± 1.6
Insulin therapy, n (%)	32 (40.0)
Hypertension, n (%)	46 (57.5)
Dyslipidaemia, n (%)	30 (37.5)
BCVA (logMAR), mean ± SD	0.34 ± 0.28
Eyes with no DR, n (%)	22 (22.0)
Eyes with mild NPDR, n (%)	18 (18.0)
Eyes with moderate NPDR, n (%)	24 (24.0)
Eyes with severe NPDR, n (%)	20 (20.0)
Eyes with PDR, n (%)	16 (16.0)
Eyes with diabetic macular oedema, n (%)	32 (32.0)
FFA-defined DMI (moderate-to-severe), n (%)	35 (35.0)

BCVA, best-corrected visual acuity; DMI, diabetic macular ischaemia; DR, diabetic retinopathy; FFA, fundus fluorescein angiography; HbA1c, glycated haemoglobin; NPDR, non-proliferative DR; PDR, proliferative DR; SD, standard deviation.

Table 2: OCT-A parameters in eyes with and without FFA-defined DMI

OCT-A parameter	Eyes without DMI (n =	Eyes with DMI (n =	p-value

	65)	35)	
FAZ area (mm²), mean ± SD	0.26 ± 0.07	0.46 ± 0.14	<0.001*
FAZ perimeter (mm), mean ± SD	2.18 ± 0.34	3.14 ± 0.62	<0.001*
FAZ circularity index, mean ± SD	0.72 ± 0.08	0.58 ± 0.12	<0.001*
SCP vessel density (%), mean ± SD	47.6 ± 3.4	40.2 ± 4.6	<0.001*
DCP vessel density (%), mean ± SD	52.4 ± 3.8	44.6 ± 5.2	<0.001*
Foveal SCP vessel density (%), mean ± SD	20.4 ± 5.6	13.2 ± 5.8	<0.001*
Parafoveal SCP vessel density (%), mean ± SD	49.8 ± 3.6	42.6 ± 4.8	<0.001*
Capillary microaneurysms, median (IQR)	2 (0–4)	8 (5–12)	<0.001*

*DCP, deep capillary plexus; DMI, diabetic macular ischaemia; FAZ, foveal avascular zone; FFA, fundus fluorescein angiography; IQR, interquartile range; SCP, superficial capillary plexus; SD, standard deviation. *Statistically significant.*

Table 3: Diagnostic performance of OCT-A FAZ area at predefined cut-offs

Cut-off (mm²)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	–LR
0.30	94.3	73.8	65.9	96.0	3.60	0.08
0.36 (Youden)	85.7	87.8	81.1	91.5	7.04	0.16
0.42	68.6	95.4	88.9	85.1	14.85	0.33

+LR, positive likelihood ratio; –LR, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

Table 4: ROC analysis of OCT-A predictors of FFA-defined DMI

Predictor	AUC	95% CI	p-value
FAZ area	0.912	0.852–0.972	<0.001*
FAZ perimeter	0.886	0.821–0.951	<0.001*
FAZ circularity (inverse)	0.842	0.770–0.914	<0.001*
SCP vessel density (inverse)	0.834	0.756–0.912	<0.001*
DCP vessel density (inverse)	0.812	0.730–0.894	<0.001*
Combined OCT-A composite score	0.928	0.876–0.980	<0.001*

*AUC, area under the receiver operating characteristic curve; CI, confidence interval; DCP, deep capillary plexus; SCP, superficial capillary plexus. *Statistically significant.*

Table 5: OCT-A parameters and DMI prevalence stratified by DR severity stage

DR stage	FAZ area (mm²)	SCP VD (%)	DCP VD (%)	DMI (FFA), n (%)
No DR (n = 22)	0.21 ± 0.04	49.4 ± 2.4	54.6 ± 2.8	0 (0.0)
Mild NPDR (n = 18)	0.26 ± 0.05	47.2 ± 2.6	52.6 ± 3.0	1 (5.6)
Moderate NPDR (n = 24)	0.32 ± 0.07	44.6 ± 3.0	48.4 ± 3.6	6 (25.0)
Severe NPDR (n = 20)	0.41 ± 0.09	41.8 ± 3.4	44.2 ± 4.0	13 (65.0)
PDR (n = 16)	0.52 ± 0.11	38.4 ± 3.8	40.6 ± 4.4	15 (93.8)
ANOVA p-value (trend)	<0.001*	<0.001*	<0.001*	—

*DCP, deep capillary plexus; DMI, diabetic macular ischaemia; DR, diabetic retinopathy; FAZ, foveal avascular zone; FFA, fundus fluorescein angiography; NPDR, non-proliferative DR; PDR, proliferative DR; SCP, superficial capillary plexus; VD, vessel density. *Statistically significant trend.*

Table 6: Two-by-two table of OCT-A vs FFA classification of DMI and agreement statistics

	FFA: DMI present	FFA: DMI absent	Total
OCT-A: DMI present (FAZ ≥ 0.36 mm²)	30 (TP)	8 (FP)	38
OCT-A: DMI absent (FAZ < 0.36 mm²)	5 (FN)	57 (TN)	62
Total	35	65	100
Cohen's kappa (95% CI), p-value	0.78 (0.66–0.90)	—	<0.001*
Bland-Altman mean bias (mm²), LoA	0.012 (–0.076 to 0.100)	—	—

*CI, confidence interval; FN, false negative; FP, false positive; LoA, limits of agreement; TN, true negative; TP, true positive. *Statistically significant.*

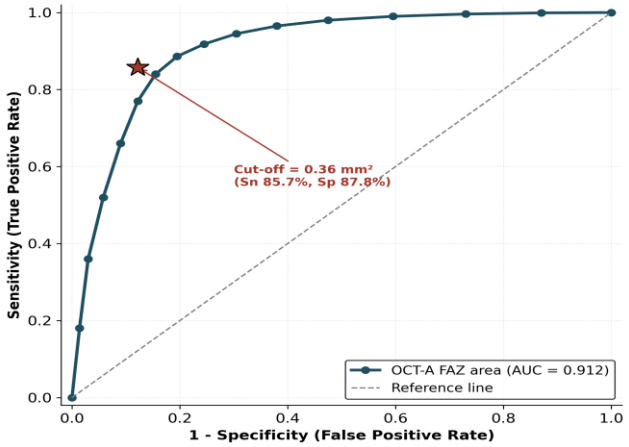

Figure 1: Receiver operating characteristic (ROC) curve of OCT-A foveal avascular zone (FAZ) area for the detection of FFA-defined diabetic macular ischaemia. Area under the curve = 0.912 (95% CI 0.852–0.972). The marked point indicates the Youden-optimal cut-off of 0.36 mm²

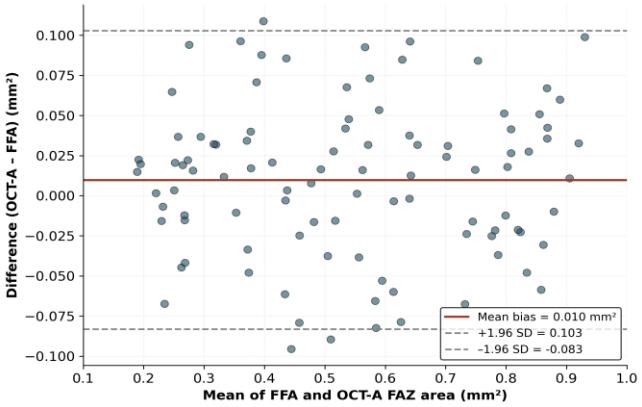

Figure 2: Bland-Altman plot comparing FAZ area measurements obtained by FFA and OCT-A. The mean bias was 0.012 mm² with 95% limits of agreement of –0.076 to 0.100 mm², indicating clinically acceptable agreement between the two modalities

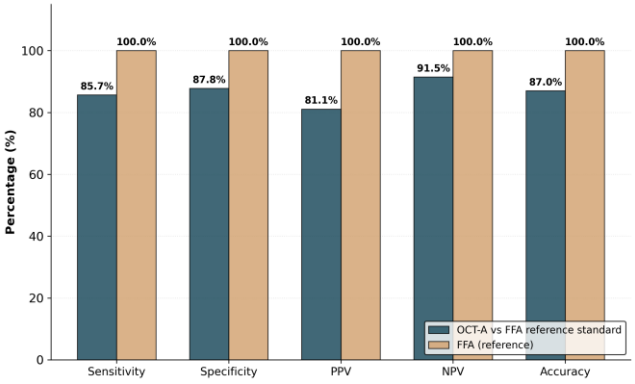

Figure 3: Diagnostic performance metrics of OCT-A at the optimal FAZ area cut-off of 0.36 mm² (sensitivity, specificity, PPV, NPV and accuracy), with FFA values displayed for reference

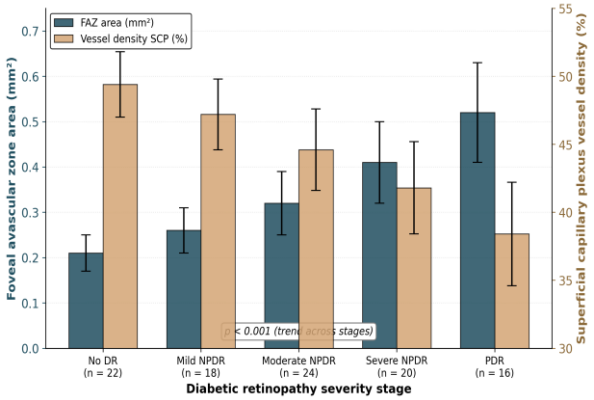

Figure 4: Foveal avascular zone (FAZ) area and superficial capillary plexus vessel density (VD-SCP) across diabetic retinopathy severity stages. Both parameters showed statistically significant trends with increasing DR severity (p < 0.001 for both)

DISCUSSION

The present prospective cross-sectional comparative diagnostic accuracy study demonstrated that OCT-A FAZ area measurements provide excellent discrimination of FFA-defined diabetic macular ischaemia, with a clinically usable Youden-optimal cut-off of 0.36 mm² yielding a sensitivity of 85.7%, specificity of 87.8%, and substantial agreement with the angiographic reference standard. The combined evaluation of FAZ area, FAZ contour and capillary plexus density marginally outperformed any single OCT-A metric, and inter-observer reproducibility was high. These findings support the routine clinical use of OCT-A as a complementary or alternative tool to FFA for the assessment of macular ischaemia in patients with diabetic retinopathy.

These results are concordant with the broader international literature. Bradley and colleagues, in a similar comparative study of 84 eyes, reported an AUC of 0.89 for OCT-A FAZ area in the detection of DMI, with optimal cut-offs and discriminative performance very close to those identified in the present cohort [11]. Hwang and co-workers similarly demonstrated that OCT-A reliably detected all FFA-evident microvascular abnormalities and revealed additional lesions in the deep capillary plexus that were not visible on FFA [12].

Couturier and colleagues, comparing OCT-A and FFA in 22 eyes, reported qualitative agreement in the assessment of capillary dropout and FAZ morphology and emphasised the additional information provided by OCT-A regarding the deep plexus [13]. Onishi and co-workers, in a methodologically rigorous evaluation, highlighted the importance of considering both the superficial and deep plexuses, including the middle capillary plexus, when assessing macular

ischaemia—a recommendation reinforced by the present finding that DCP vessel density was as informative as SCP density [14].

The progressive enlargement of the FAZ and reduction of capillary plexus density with increasing DR severity observed in the present study mirrors the findings of Agemy and colleagues, who reported a clear quantitative gradient of perfusion abnormalities across DR stages and identified OCT-A as a sensitive marker of subclinical microvascular disease [15].

OCT-A also offers important practical advantages over FFA. It is non-invasive, dye-free, rapid (each eye is imaged in less than 30 seconds), and can be repeated at every clinic visit without the cumulative risk of intravenous fluorescein. The technique provides depth-resolved visualisation of the superficial, deep and choriocapillaris plexuses, yields reproducible quantitative metrics, and is well suited to longitudinal follow-up of patients with diabetic retinopathy and other macular vascular disorders [16]. The acquisition workflow is also more amenable to delegation to trained ophthalmic technicians, with the potential to scale OCT-A use widely in outpatient and community-based settings.

Several limitations of OCT-A nevertheless warrant attention. The standard 3 × 3 mm scan field is restricted to the central macula and may miss peripheral or extramacular ischaemia—a limitation reflected in the present study by the small number of false-negative cases in which DMI was located outside the central macular field [17]. Image quality is also vulnerable to motion artefact, segmentation errors, projection artefact from superficial vessels onto deeper layers, and reduced signal in eyes with media opacity [18]. Spaide and colleagues have systematically described these artefacts and emphasised the importance of meticulous quality control before interpretation, principles that were adhered to in the current study [19].

The strengths of the present study include its prospective design, consecutive enrolment, same-day imaging by both modalities, blinded image interpretation, use of validated quantitative OCT-A metrics, and high inter-observer reproducibility. Several limitations should also be acknowledged. The single-centre nature of the study and the modest sample size limit external generalisability. The 3 × 3 mm OCT-A scan field, while standard, does not allow for the detection of peripheral ischaemia visible on wide-field FFA. Eyes with significant diabetic macular oedema or media opacity were under-represented, since these conditions degrade OCT-A image quality and may bias the apparent diagnostic accuracy. Finally, longitudinal data regarding the relationship between baseline OCT-A metrics and visual outcomes were beyond the scope of the present cross-sectional analysis.

CONCLUSION

OCT-A FAZ area measured on a 3 × 3 mm macular scan provides excellent discrimination of FFA-defined diabetic macular ischaemia, with an area under the ROC curve of 0.912 and a clinically usable Youden-optimal cut-off of 0.36 mm² yielding a sensitivity of 85.7% and specificity of 87.8%. Inter-modality agreement with FFA was substantial (Cohen's kappa 0.78), and OCT-A vessel density and FAZ morphology metrics demonstrated consistent quantitative trends with diabetic retinopathy severity. These findings, together with the non-invasive, dye-free, rapid and reproducible nature of OCT-A, support its routine use as a complementary or alternative tool to fluorescein angiography for the assessment of macular ischaemia in patients with diabetic retinopathy. Larger multicentre studies and longitudinal evaluations of OCT-A metrics in relation to functional outcomes are warranted to define the optimal role of this technology in routine ophthalmic practice.

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