Contribution of optical coherence tomography angiography OCT-A in diabetic maculopathy

Ahmed Mahjoub, Ines Cherni, Oumayma Khayrallah [*], Nadia Ben Abdesslam, Anis Mahjoub, Romdhane Anas, Mohamed Ghorbel, Hachmi Mahjoub, Leila Knani, Fethi Krifa

Department of Ophtalmology, Farhat Hached Hospital, Sousse, Tunisia

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ABSTRACT

Introduction: Diabetic retinopathy (DR) increases the risk of blindness by 25 times. Advanced researchs are justified for better management, leading to the role of Optical Coherence Tomography-Angiography (OCT-A), a new non-invasive imaging technique exploring retinal vascularization.
Our purpose is to identify microvascular macular anomalies of DR on OCT-A with qualitative and quantitative evaluation of their impact on retinal vascularization.
Patients and methods: This is a descriptive cross-sectional study where 120 eyes of 66 diabetic patients were enrolled. All patients were diabetic and went through OCT-A imaging.
Results: Microanevrysms were identified in both superficial capillary plexus (SCP) and deep capillary plexus (DCP) where they were more frequently visualized. Macular edema was present in 16,7% of cases in the SCP, and in 30% in DCP. Edema spaces were more frequently present in DCP (p < 0,05). Capillary nonperfusion areas were identified in 82,5% of cases in SCP and in 60% of cases in DCP. The main peri-foveal vascular density was 18,95 ± 5,37%. The main surface of foveal avascular zone (FAZ) in the SCP was 462,52 μm^2 and was 555,04 ± 329,11 μm^2 in the DCP where it was larger.
Conclusion: OCT-A is a modern imaging tool that could be used for the diagnosis and monitoring of DR as well as the understanding of its pathophysiology.

1. Introduction

While progress in exploration is bringing non-invasive imaging methods to the forefront, ophthalmology has seen the development of optical coherence tomography angiography (OCT-A). And since the number of patients with diabetic retinopathy (DR) is increasing [1,2], advanced researchs are required for a diagnostic and therapeutic progress.

2. Methods

This is a descriptive cross-sectional study. It involved 120 eyes of 66 patients who presented to the ophthalmology department at Farhat Hached Hospital in Sousse (Tunisia) between April and December 2018. All procedures performed in this study were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Our study is registered in Research Registry and the number of the study is 7057.

The work has been reported in line with the STROCSS criteria [3].

Written informed consent was obtained from the patient for publication of this article and accompanying images. All included patients have diabetes Mellitus.

We excluded: All patients with fundus pathology related to a disease other than diabetes and patients whose OCT-A was of poor quality.

The collected data included epidemiological characteristics (age, sex), history, diabetes characteristics (type, duration, treatment), as well as ophthalmological clinical data: visual acuity (VA), anterior segment, vitreous status and fundus examination. OCT and OCT-A were performed by the Topcon® DRI OCT Triton™ Swept Source OCT.

In OCT-A a qualitative analysis was carried out on the 6 × 6 mm images, where the translation of elementary microvascular anomalies of the DR was studied, in addition to a quantitative analysis, which included the automatic evaluation of the vascular density (VD) in the

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* Corresponding author. Ophtalmology department, Farhat Hached Hospital of Sousse, Faculty of medicine of Sousse, Tunisia.
E-mail address: oumeyma.khayrallah1506@gmail.com (O. Khayrallah).

superficial plexus (6 × 6 mm images) and the calculation of the FAZ surface (on the 3 × 3 mm images) in the superficial capillary plexus (SCP) and the deep capillary plexus (DCP) (by manual tracing).

Quantitative variables were expressed as averages ± standard deviation by specifying minimum and maximum values or medians. Qualitative variables were expressed by number and percentage. The VA was expressed in decimal VA and log MAR. In all statistical tests, the significance level was set at p = 0.05 between two groups being compared. The degree of correlation between two quantitative variables was assessed by the Pearson correlation coefficient 'r'. If ┃r┃ < 0.3 the correlation was considered low, and if ┃r┃ ≥ 0.5, the correlation was good. And in case of invalidity, the correlation coefficient of the Spearman ranks was determined. SPSS v23 was used for data analysis.

3. Results

120 eyes of 67 diabetic patients (44.8% female) were included in our study. The average age was 58.19 years (±9.46 years). The average duration of diabetes was 9.45 years.

The mean VA by far was 4.6/10 ± 0.27/10 (corresponding to +0.48 log MAR ± 0.48), it varied from 0.05/10 to 10/10 (+2.3 to 0 log MAR) and was greater than 5/10 in 50.83% of eyes.

In structural OCT, the mean central macular thickness (CMT) was 288.29 ± 84.65 μm with extremes ranging from 187 to 547 μm.

We were able to visualize the basic lesions of DR with OCT-A, in both superficial and deep plexus. The results of these observations are noted in Table 1.

There were a total of 42 new vessels (NV) in SCP and 22 in DCP. Five NVs in DCP were also visible in the superficial plexus, and 17 were identifiable in the deep network only (Fig. 1).

In the group of patients with diabetic macular edema (DME) in OCT-A (Fig. 2), the mean number of microaneurysms (SCP = 6.72 ± 7.94 and DCP = 10.06 ± 8.37) was higher than in those with DR without edema (SCP = 3.69 ± 3.84 and DCP = 3.93 ± 5.11), especially in the DCP, with a statistically significant difference between the two groups in both plexuses (p = 0,013 in SCP and 0,001in the DCP).

Among the eyes with edema spaces in the SCP, 19 eyes were associated with non perfusion area (95%), and for those with DME in the DCP, 35 eyes were associated with non perfusion area (97.22%).

On the other hand, the alteration of the normal vortex architecture of DCP was noted in 50 eyes (41.7%). In the patients with edema spaces in the DCP, 29 eyes (58%) had an altered vortex structure. The preservation of this structure was negatively correlated with the presence of edema with a significant difference (p < 0.05; r = −0.51).

The FAZ was studied in the SCP in 113 eyes (94.17%). It was ruptured in 51 eyes (42.5%). The study was not possible for 7 eyes (5.83%) among which were noted: 4 cases of cystoid spaces. In the DCP: The FAZ was identifiable in 93 eyes (77.5%); of the remaining 27 eyes, 21 had central cystoid spaces (77%), the rest were the site of artifacts or significant architectural disorganization. The results of the FAZ measurement are detailed in Table 2.

In the group of patients with DME at OCT-A, the FAZ was wider compared to the DR group without edema in both the SCP (FAZ = 472.872 (edema group) vs. 399.779 μm² (no edema group)) and the DCP (571.262 (edema group) vs. 551.844 μm² (no edema group)) without a statistically significant difference (P = 0,24 in SCP and 0,8 in DCP). The FAZ in DCP was larger.

The VD was studied at the level of the superficial plexus. The measurements of the different VD territories are detailed in Table 2. In the group of patients with DME at the OCT-A, the perifoveolar VD of the SCP was lower (18 ± 4.69) than in the group with DR without edema (21.18 ± 6.22) with a statistically significant difference (P = 0.003).
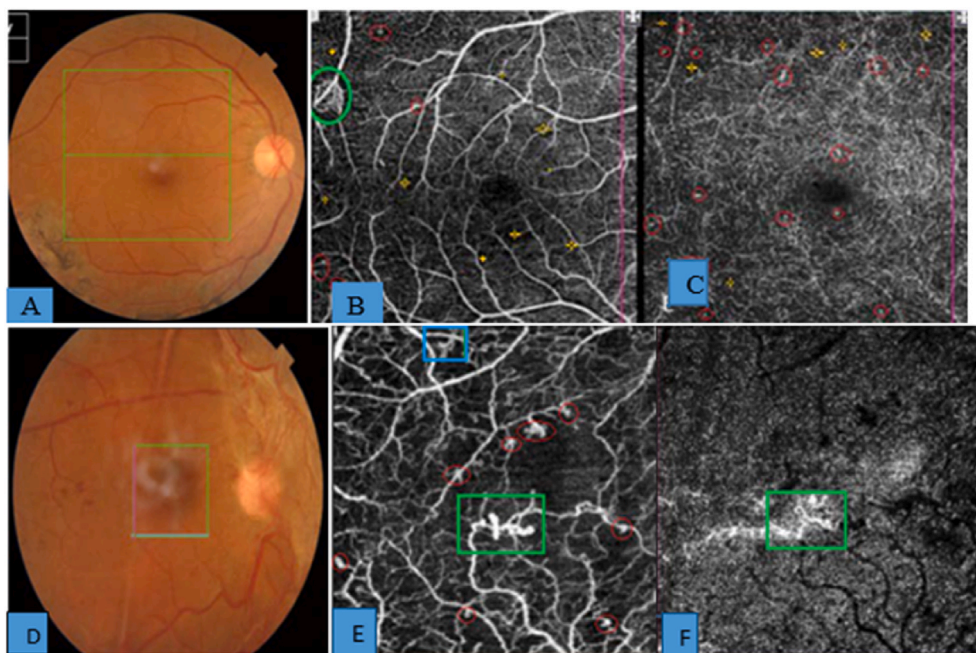
Concerning the clinical data, we found a correlation between the presence of OCT-A edema spaces in the SCP and the DCP with VA (p < 0.05). The number of new vessels in SCP and DCP in our series was also correlated with lower VA (p = 0.04; r = −0.26 in both plexuses). On the other hand, the perifoveolar VD of SCP had a moderately positive correlation with VA (p = 0.009; r = 0.23) and a moderately negative correlation with log MAR VA (p = 0.001; r = −0.31). VA was also correlated with FAZ rupture (p = 0.001), it was lower in patients with a larger FAZ in SCP and DCP (p = 0.014 and 0.001 respectively and r < 0 for both).

And about the relationship between the DR stage and the anomalies found at OCT-A, the results are detailed in Table 3. Microvascular abnormalities were significantly correlated with DR stage in both SCP and DCP.

3.1. MA:microanevrysm

The therapeutic modalities of DR and DME had not influenced the qualitative and quantitative data of OCT-A in either the SCP or DCP.

On the other hand, it was noted that ellipsoid rupture as well as alteration of the external retina in structural OCT was correlated with the presence of areas of vascular non-perfusion in DCP in OCT-A (p = 0.043 for both; r respectively = 0.186 and 0.185). Furthermore, among the microvascular lesions in DR, CMT was significantly correlated with the presence of microaneurysms in DCP (p = 0.023; r = 0.21), but not in the superficial one (p = 0.6). In addition, in our series the mean CMT in patients with altered DCP architecture (388 ± 138.59 μm) was higher

Table 1
Qualitative anomalies in OCT-A.

	SCP			DCP			P
	Total number of lesions in all eyes	Number of eyes (N)	Percent of eye (%)	Total number of lesions in all eyes	Number of eyes (N)	Percent (%)	
Micro-anévrysmes	538	90	75	754	95	79,16	0.004
Superior		11	9,17		17	14,16	
Inferior		2	1,67		2	1,66	
Nasal		6	5		11	9,16	
Temporal		3	2,5		11	9,16	
Supero-temporal		2	1,67		6	5	
Infero-nasal		1	0,83		2	1,66	
Supero-nasal		1	0,83		–	–	
Infero-temporal		3	2,5		–	–	
perifoveolar		19	15,83		46	38,33	
edema spaces		20	16,7		36	30	<0,05
Central edema		8	6,67		17	14,16	
IRMA	58	32	26,66	24	17	14,16	<0,05
New vessel	42	20	16,7	22	14	11,66	
Non perfusion area		99	82,5		72	60	

Fig. 1. PDR at OCT-A: A + B + C: right eye images of patient D.D, aged 36 years old, with type 1 diabetes for 21 years; A: photo of the fundus showing photocoagulated DR; **B:** 6 × 6 mm image of OCT-A at the SCP showing a preretinal new vessel (green circle) not clinically visible, as a prominent hyper-reflective high-flux vascular loop of complex architecture whose morphology is clearly identifiable and confined to the SCP, in addition to some micro-aneurysms (red circles) and nonperfusion areas (yellow star); C: 6 × 6 mm image of OCT-A at DCP showing microanevrysms, non perfusion areas, and altered vortex architecture. **D + E + F:** right eye images of the 72-year-old patient (M.H) with type 2 diabetes for 26 years; D: fundus image of the patient showing severe PDR; E: 6 × 6 mm OCT-A image at the SCP showing non perfusion areas, microanevrysm, IRMA (blue square) as well as a new vessel (green square); F: architectural alteration with projection artifact, hyper-reflectivity of the new vessel of the SCP also visible at this level. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
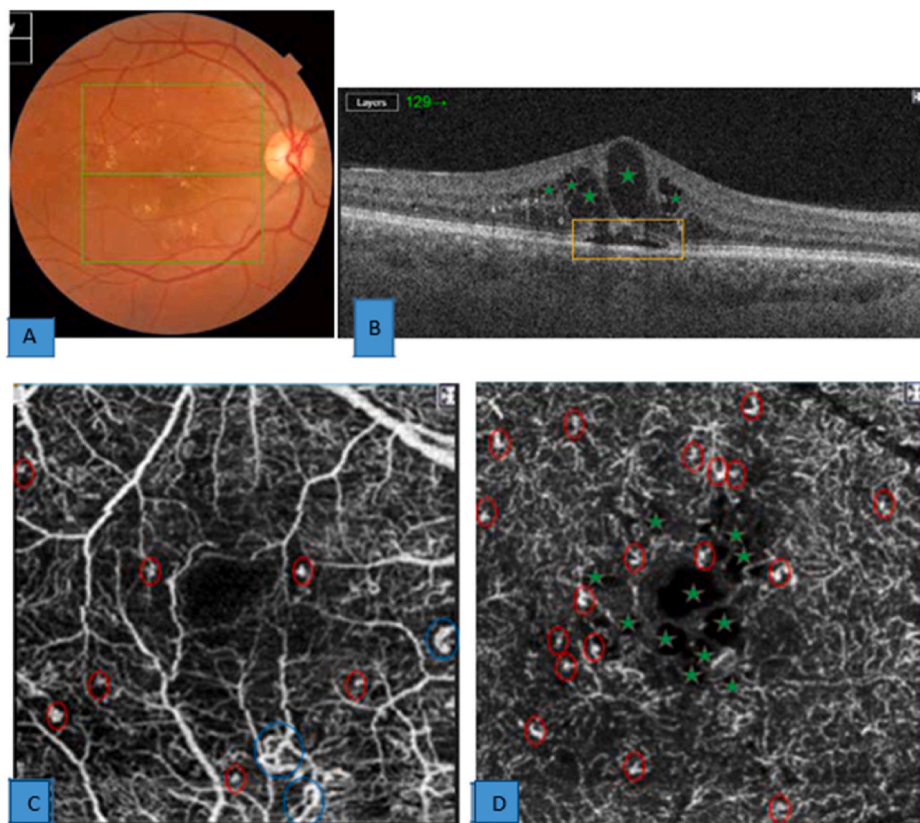
Fig. 2. DME at OCT-A: A: fundus photo of the right eye of patient R.Z aged 51 years with type 2 diabetes discovered 2 years ago showing moderate NPDR with severe DME; B: Structural macular OCT showing DME with loss of foveolar depression, cystoid spaces (green stars) and serous retinal datachment (yellow square); C: 3 × 3 mm OCT-A image at SCP showing several non perfusion areas, micro-aneurysms (red circles), IRMA (blue circle) as well as an enlarged FAZ; D: 3 × 3 mm image at the DCP showing central DME with sharp, rounded dark-coloured hyposignal boundaries, associated with multiple micro-aneurysms and nonperfusion area, the vortex architecture is no longer preserved. The FAZ boundaries at this level can no longer be assessed because of the DME. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

than those with preserved architecture (287.34 ± 83.35 μm) with a statistically significant difference ($p < 0.05$). The FAZ study was more difficult for patients with a higher CMT, for whom the mean CMT was 381.7 ± 113.93 μm significantly higher than for patients with a studyable FAZ (259.65 ± 47.28 μm $p < 0.05$). CMT was also correlated with the rupture of the FAZ ($p = 0.002$). VD was, however, negatively correlated with CMT ($p < 0.05$, $r = -0.38$).

Table 2
Quantitative anomalies in OCT A.

	Results	P
FAZ in SCP (µm2)	462,52 ± 232,18	
(N=113)	(128,82–1686,1)	<0,001
FAZ in DCP (µm2)	555,04 ± 329,11	
(N=91)	(149,25–2404,67)	
perifoveolar VD (mm -1)	18,95 ± 5,37	
(N=118)	(1,35–38,71)	
superior VD (mm -1)	43,7 ± 5,11	
(N=118)	(10–52,29)	
inferior VD (mm -1)	42,96 ± 5,46	
(N=118)	(13,98–57,35)	
nasal VD (mm -1)	42,43 ± 3,86	
(N=117)	(31,16–51,54)	
temporal VD (mm -1)	43,67 ± 3,71	
(N=118)	(35,62–53,04)	

4. Discussion

4.1. Elementary lesions of DR

Microaneurysm, an early sign of DR, is a lesion that appears in OCT-A as a generally rounded, saccular signal [4–6]. According to our results, OCT-A has the advantage of locating these lesions at their exact intra-retinal depths: microaneurysms were visible in both SCP and DCP. They were significantly more numerous in the latter (p = 0.004), in accordance with the litterature [7–9]; this suggests that microaneurysms develop mainly in the deep capillary network, as already shown in histology [10]. Furthermore, we have noted that most microaneurysms are located at the edge of a non-perfused capillary zone as reported by the work of Ishibazawa, Peres and Hasegawa [7,9,11] and are therefore indirect signs of retinal ischemia. It was also described that these lesions sometimes surround the FAZ [7,12,13]. In our series, microaneurysms were predominant in the perifoveolar region in the majority of cases.

IRMAs are complex, highly decorelated vascular structures that are visible near non-perfused areas. In our series, IRMAs were noted in both SCP and DCP, they were significantly predominant in SCP (53 in SCP vs 26 in DCP). Similar results were found by Ishibazawa and al [7] but Lupidi and al [14] found a predominance of IRMAs in DCP. Pan reported that IRMAs would have venous origin and drainage, and develop from the internal plexiform layer (boundary between SCP and DCP), the layer of ganglion cells, or optical fiber (SCP), which shows that these lesions can be identified in both plexuses. Preretinal new vessels are visible in OCT-A as hyper-reflective, high-flux lesions, with complex and disorganised architecture and variable calibre [15]. Pan had thus established a classification [16] in which the starting layer of NV type 1 was the most superficial, type 2 was the deepest, and type 3 was the intermediate. This distribution consolidates our results, and shows that NVs are visible in both plexuses, and that some can be identified in both at the same time.

4.2. Visualization and quantification of macular ischemia

4.2.1. Areas of retinal non-perfusion

OCT-A finds a modification of both capillary networks. At the SCP level, DR causes a capillary depletion with non-perfusion zones, which can be visualized very well at the OCT-A level [17]. In DCP, these areas are less well delimited, and the DR induces an alteration of the normal capillary vortices [18].

In our series, in SCP, zones of vascular non-perfusion were identified in 99 eyes (82.5%). In DCP, they were present in 72 eyes (60%). The non perfusion areas were mostly bordered by microvascular lesions according to the literature [7,9,11,15]. In Couturier's series, these territories were present in all eyes in OCT-A in SCP; in DCP, they were present in only about 35% (7/20) of cases [8] with capillary vortex alteration in all eyes. The reason for such a discrepancy in the presentation of non-perfusion between SCP and DCP is not yet well explained

Table 3
Anomaly of SCP and DCP depending on the stage of DR.

		mild NPDR (n=17)	Moderate NPDR (n=24)	Severe NPDR (n=28)	PDR (n=21)	P
MA in SCP	Average eye	3,53 ± 3555 15 (88,23%)	4,95 ± 6070 21 (87,5%)	5,31 ± 3380 26 (92,85%)	7,15 ± 5383 19 (90,47%)	<0,05
MA in DCP	Average eye	4,80 ± 4195 16 (94,11%)	6,83 ± 6228 23 (95,83%)	7,82 ± 6464 27 (96,42%)	9,63 ± 7897 19 (90,47%)	<0,05
IRMA in SCP	average eye	0,29±,772 3 (17,64%)	0,54 ± 1285 7 (29,16%)	0,61±,875 13 (46,42%)	1,10 ± 1729 9 (42,85%)	0,008 <0,05
IRMA in DCP	average eye	0,18 ± 0,728 1 (5,88%)	0,21 ± 0,588 3 (12,5%)	0,29 ± 0,535 7 (25%)	0,38 ± 0,669 6 (28,57%)	0128 <0,05
NV in SCP	average Eye	0	0,21 ± 0,658 3 (12,5%)	0,32 ± 0,548 8 (28,57%)	1,33 ± 2352 9 (42,85%)	<0,05
NV in DCP	Average Eye	0 0	0,17 ± 0,482 3 (12,5%)	0,46 ± 0,881 8 (28,57%)	0,24 ±0,7 3 (14,28%)	0,019 <0,05
Nonperfusion area of SCP		17 (100%)	24 (100%)	28 (100%)	21 (100%)	<0,05
Nonperfusion area of DCP		14 (82,35%)	15 (62,5%)	17 (60,71%)	20 (95,23%)	<0,05
vortex alteration		7 (41,17%)	9 (37,5%)	12 (42,85%)	21 (100%)	<0,05
VD perifoveolar in SCP		18,41± 3187	18,377± 6102	18,324± 5520	17,996± 4125	0,032
FAZ in SCP		409,240± 144,669	442,189± 153,799	528,242± 274,418	583,092± 294,498	0,002
FAZ in DCP		487,363± 185,506	584,479± 419,428	641,932± 446,046	729,643± 216,027	0,016
FAZ rupture		5 (29,41%)	14 (58,33%)	18 (75%)	17 (80,95%)	<0,05

even histologically [7]. According to Bonnin, a disorganization of the deep plexus is systematic, and the normal vortex architecture is no longer respected [17], the vortices are hardly visible, and increasingly absent as the DR progresses. In our series, the normal vortex architecture was altered for 50 eyes (41.7%), with a strong negative correlation with the stage of DR (p < 0.05, r = −0.62) (Table 3).

Several studies on DR based on OCT-A suggest that DCP was affected more severely than SCP [7,8,12,19–21,27,36,45]. A correlation was found between the vascular changes observed in OCT-A, photoreceptor interruption and the severity of DR [22,23]. In our series, the presence of areas of vascular non-perfusion at DCP levels in OCT-A was correlated with ellipsoid rupture (p = 0.043; r = 0.186) and alteration of the external retina (p = 0.043; r = 0.185) in structural OCT. This would reflect the association of these anatomical lesions with capillary non-perfusion of the deep retina in ischemic maculopathy.

4.2.2. Vascular density (VD)

In our series, the VD was studied at the level of the SCP (Table 2). It was decreased in all territories in agreement with Agemy's results [25]. In the literature, VD values were negatively correlated with the severity of diabetes [26–28] as well as in our series (p = 0.036) (Table 3). On the other hand, the results diverge regards to the relationship between VD and VA. In Hwang's series [30], no correlation was found between perifoveolar and parafoveolar VD and VA. On the other hand, in a larger study by Samara [29], a statistically significant negative correlation was found between log MAR (VA) and VD in SCP and DCP, however Durbin found a weak negative correlation between VD in SCP with VA [24], as did Attaallah who, on the other hand, found no correlation with VD in DCP [31]. In our series the perifoveolar VD in SCP had a moderately positive correlation with VA (p = 0.009; r = 0.23) and a moderately negative correlation with log MAR (VA) (p = 0.001; r = −0.31). Adding a quantitative parameter to the current stage of DR makes the stage assessment a measurable parameter. This would make it possible to identify patients at risk, predict therapeutic efficacy and help in the follow-up of diabetic patients.

4.2.3. The central avascular zone (ZAC)

The underlying pathophysiology of FAZ enlargement in the DR is most likely related to microinfractures in the surrounding vascular arches [33,34] and loss of capillaries adjacent to the vessels [14].

Lupidi andt al [14] as well as Attaallah and al [31] reported a statically significant difference in the area of the FAZ between the superficial and deep plexus where it is wider. Similar results were found in our series (with p < 0.001 and r = 0.95). This was explained by the difference in vascular architecture which is terminal at the DCP as opposed to the SCP which has a continuous capillary ring around the FAZ.

The size of the FAZ (in SCP and DCP) has been reported in a few studies to be associated with function and visual acuity [35–38]. However, this correlation was not proven in another series [30]. In our series, both FAZ enlargement and FAZ disruption were correlated with visual acuity with a statistically significant difference (p respectively = 0.014 and 0.001). This is consistent with previous results based on clinical and angiographic findings [33,39].

However, the size of the FAZ in OCT-A is believed to play a limited role in predicting VA in eyes with DR, as inter-individual variation in the surface and morphology of the FAZ has been observed [40–43] and was attributed to a complex difference in foveolar development with an increase in the length of its axis after the formation of the FAZ [44].

In addition, FAZ measures tended to increase with the progression of DR in most studies [12,28,36,46–48]. In our series, this widening in both SCP and DCP was proportional to the severity of diabetic retinopathy (p 0.002 and 0.016 respectively). The FAZ was wider in the advanced stages of DR (Table 3). These results confirm studies carried out with angiography several decades earlier [49] where microvascular changes and macular ischemia are pronounced in the advanced stages of DR [15].

4.3. Diabetic macular edema

DME appears in OCT-A as intraretinal space or hyporeflective cysts, devoid of signal, with rounded and smooth hyperreflective edges that do not follow the boundaries of neighboring capillaries [18].

In our series, microaneurysms are more numerous when associated with edema, in fact, the mean number of microaneurysms was higher in patients with DME compared to those with DR without DME, with a statistically significant difference between the two groups in the SCP and in the DCP. Microaneurysms associated with DME were also found to be more frequent in the DCP in congruence with the results of Peres [11]. CMT was also positively associated with the presence of microaneurysms in DCP in our series (P = 0.023; r = 0.21), in accordance with hasegawa's results [9].

Furthermore, Mané had suggested that for DME fluid would accumulate preferentially in areas of vascular depletion particularly in DCP [50]. In our series, it was noted that the presence of edema in OCT-A was associated with the presence of capillary non perfusion areas in 95% of cases in SCP and in 97% of cases in DCP.

Quantitatively, the VD of SCP was lower in the DR group with DME (18 ± 4.69) than in the group without edema territories (21.18 ± 6.22) with a statistically significant difference (P < 0.05) at the perifoveolar level. The presence of edema spaces in the OCT-A would therefore be correlated with a lower VD. In agreement with the work of Kim and al [26] and Tang and al [51].

It should be noted that in our series a correlation between VD and CMT was found (p < 0.05 and r = 0.38) in conformity with Dimitrova's results [32].

It was also reported in the Mané series, which included patients with DME, that the normal vortex vascular structure of DCP was altered in all patients [50]. In our series the impairment of this architecture was correlated with the mean CMT, which in patients with altered DCP architecture (388 ± 138.59 μm) was higher than in those with preserved architecture (287.34 ± 83.35 μm) with a statistically significant difference (p < 0.05). Vortex architecture was absent in 59% of patients with DME spaces in OCT-A, and the association of normal architecture with the cystoid spaces was negatively significant.

On the other hand, the distribution of cystoid spaces in our series was predominantly central, and this was a limitation to the estimation of the FAZ measurement especially in DCP where edema was predominant.It is important to note that the presence of DME influences the reproducibility and measurement efficiency of the FAZ in the SCP and the DCP [14,17,20,25,49].

Furthermore, we noted that the FAZ was wider in the DR group with DME compared to the DR group without DME both in the SCP (472,872 vs. 399,779 μm² respectively) and in the DCP (571,262 vs. 551,844 μm² respectively) without statistically significant difference. The FAZ in DCP was larger. Peres and al [11] and Di and al [47] also found that the DME was associated with a wider FAZ in both the superficial and deep plexus. Attaallah approved this result for the SCP only [31]. The angiography had already shown that the FAZ was wider in patients with DME compared to healthy controls [39,40]. As OCT-A is non-invasive and reproductible, it can identify retinal vascularization and microanatomy simultaneously and is able to visualize the capillary network in depth.

5. Conclusion

Our study showed that retinal microvascular abnormalities were observed in all stages of DR. It also showed that the presence of these abnormalities was proportional to the severity of DR and more pronounced in the presence of DME, and that DCP was more severely affected than SCP. In addition, the assessment of macular ischemia could be based on the identification of areas of vascular rarefaction, the quantitative assessment of VD and the qualitative and quantitative study of the FAZ.

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Ethical approval

Approval has been given.

Consent

Oral informed consent was obtained from the subjects to participate in this study.

Author contribution

Ahmed Mahjoub: Editing of the manuscript. Ines Cherni: Conceptualization, Data support, data collection, Editing of manuscript, investigation, writing original draft. Oumayma Khayrallah: Writing the paper. Nadia Ben Abdesslam: Examination and correction. Anis Mahjoub: Data collection. Anas Romdhane: Data collection. Mohamed Ghorbel: Manuscript correction, supervision of the manuscript. Hachemi Mahjoub: Supervision of the manuscript, manuscript correction. Leila Knani: manuscript correction, supervision of the manuscript. Fathi Krifa: Study design.

Registration of research studies

1 Name of the registry: Research registry
2 Unique Identifying number or registration ID: 7057
3 Hyperlink to your specific registration (must be publicly accessible and will be checked):https://www.researchregistry.com/browse-the-registry#home/registrationdetails/6117a415d4bcc6001fe6fcd0/

Guarantor

Oumayma Khayrallah, Ines Cherni.

Declaration of competing interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102904.

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References

[1] K.L. Alexander, PRIMARY CARE OF THE POSTERIOR SEGMENT, 2ND ED., vol. 71, Optometry and Vision Science, juin 1994, p. 410, 6.

[2] S. Ayed, in: Contribution à l'étude de la rétinopathie diabétique en tunisie, Thèse médicale Tunis, Tunisie), 1980, p. n°484.

[3] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, for the STROCSS Group, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in Surgery, Int. J. Surg. 72 (2019) 156–165.

[4] J.S. Corcoran, K. Moore, O.P. Agarawal, D.F. Edgar, J.S. Yudkin, Visual acuity screening for diabetic maculopathy, Pract Diab Int 2 (6) (nov 1985) 30–32.

[5] M. Shahidi, Retinal thickness analysis for quantitative assessment of diabetic macular edema, Arch. Ophthalmol. 109 (8) (1 août 1991) 1115.

[6] F. Forooghian, P.F. Stetson, S.A. Meyer, E.Y. Chew, W.T. Wong, C. Cukras, et al., Relationship between photoreceptor outer segment length and visual acuity in diabetic macular edema, Retina 30 (1) (janv 2010) 63–70.

[7] A. Ishibazawa, T. Nagaoka, A. Takahashi, T. Omae, T. Tani, K. Sogawa, et al., Optical coherence tomography angiography in diabetic retinopathy: a prospective pilot study, Am. J. Ophthalmol. 160 (1) (juill 2015) 35–44.e1.

[8] A. Couturier, V. Mané, S. Bonnin, A. Erginay, P. Massin, A. Gaudric, et al., Capillary plexus anomalies IN diabetic retinopathy ON optical coherence tomography angiography, Retina 35 (11) (nov 2015) 2384–2391.

[9] N. Hasegawa, M. Nozaki, N. Takase, M. Yoshida, Y. Ogura, New insights into microaneurysms in the deep capillary plexus detected by optical coherence tomography angiography in diabetic macular edema, Invest. Ophthalmol. Vis. Sci. 57 (9) (01 2016) OCT348–355.

[10] J. Moore, S. Bagley, G. Ireland, D. McLeod, M.E. Boulton, Three dimensional analysis of microaneurysms in the human diabetic retina, J Anat. janv 194 (Pt 1) (1999) 89–100.

[11] M.B. Peres, R.T. Kato, V.F. Kniggendorf, E.D. Cole, S. Onal, E. Torres, et al., Comparison of optical coherence tomography angiography and fluorescein angiography for the identification of retinal vascular changes in eyes with diabetic macular edema, Ophthalmic Surg Lasers Imaging Retina 47 (11) (01 2016) 1013–1019.

[12] Y. Miwa, T. Murakami, K. Suzuma, A. Uji, S. Yoshitake, M. Fujimoto, et al., Relationship between functional and structural changes in diabetic vessels in optical coherence tomography angiography, Sci. Rep. 6 (2) (28 2016), 90-64.

[13] S. Yu, J. Lu, D. Cao, R. Liu, B. Liu, T. Li, et al., The role of optical coherence tomography angiography in fundus vascular abnormalities, BMC Ophthalmol. 13 juill 16 (2016) 107.

[14] M. Lupidi, G. Coscas, F. Coscas, T. Fiore, E. Spaccini, D. Fruttini, et al., Retinal microvasculature in nonproliferative diabetic retinopathy: automated quantitative optical coherence tomography angiography assessment, Ophthalmic Res. 58 (3) (2017) 131–141.

[15] A. Ishibazawa, T. Nagaoka, H. Yokota, A. Takahashi, T. Omae, Y.-S. Song, et al., Characteristics of retinal neovascularization in proliferative diabetic retinopathy imaged by optical coherence tomography angiography, Invest. Ophthalmol. Vis. Sci. 57 (14) (01 2016) 6247–6255.

[16] J. Pan, D. Chen, X. Yang, R. Zou, K. Zhao, D. Cheng, et al., Characteristics of neovascularization in early stages of proliferative diabetic retinopathy by optical coherence tomography angiography, Am. J. Ophthalmol. 192 (1 août 2018) 146–156.

[17] S. Bonnin, V. Mané, A. Couturier, M. Julien, M. Paques, R. Tadayoni, et al., New insight into the macular deep vascular plexus imaged BY optical coherence tomography angiography, Retina 35 (11) (nov 2015) 2347–2352.

[18] T.E. de Carlo, A.T. Chin, T. Joseph, C.R. Baumal, A.J. Witkin, J.S. Duker, et al., Distinguishing diabetic macular edema from capillary nonperfusion using optical coherence tomography angiography, Ophthalmic Surg Lasers Imaging Retina 47 (2) (Févr 2016) 108–114.

[19] D.A. Salz, T.E. de Carlo, M. Adhi, E. Moult, W. Choi, C.R. Baumal, et al., Select features of diabetic retinopathy on swept-source optical coherence tomographic angiography compared with fluorescein angiography and normal eyes, JAMA Ophthalmol 134 (6) (1 juin 2016) 644–650.

[20] J.M. Simonett, F. Scarinci, F. Picconi, P. Giorno, D. De Geronimo, A. Di Renzo, et al., Early microvascular retinal changes in optical coherence tomography angiography in patients with type 1 diabetes mellitus, Acta Ophthalmol. 95 (8) (déc 2017) e751–e755.

[21] B. Dupas, W. Minvielle, S. Bonnin, A. Couturier, A. Erginay, P. Massin, et al., Association between vessel density and visual acuity in patients with diabetic retinopathy and poorly controlled type 1 diabetes, JAMA Ophthalmol 136 (7) (01 2018) 721–728.

[22] Y. Dodo, T. Murakami, K. Suzuma, S. Yoshitake, T. Yoshitake, K. Ishihara, et al., Diabetic neuroglial changes in the superficial and deep nonperfused areas on optical coherence tomography angiography, Invest. Ophthalmol. Vis. Sci. 58 (13) (01 2017) 5870–5879.

[23] M. Al-Sheikh, H. Akil, M. Pfau, S.R. Sadda, Swept-source OCT angiography imaging of the foveal avascular zone and macular capillary network density in diabetic retinopathy, Invest. Ophthalmol. Vis. Sci. 57 (8) (01 2016) 3907–3913.

[24] A.Y. Kim, Z. Chu, A. Shahidzadeh, R.K. Wang, C.A. Puliafito, A.H. Kashani, Quantifying microvascular density and morphology in diabetic retinopathy using spectral-domain optical coherence tomography angiography, Invest. Ophthalmol. Vis. Sci. 57 (9) (1 juill 2016) OCT362–O370.

[25] S.A. Agemy, N.K. Scripsema, C.M. Shah, T. Chui, P.M. Garcia, J.G. Lee, et al., Retinal vascular perfusion density mapping using optical coherence tomography angiography IN normals and diabetic retinopathy patients, Retina 35 (11) (nov 2015) 2353–2363.

[26] A.Y. Kim, Z. Chu, A. Shahidzadeh, R.K. Wang, C.A. Puliafito, A.H. Kashani, Quantifying microvascular density and morphology in diabetic retinopathy using spectral-domain optical coherence tomography angiography, Invest. Ophthalmol. Vis. Sci. 57 (9) (juill 2016) OCT362–O370.

[27] A. Carnevali, R. Sacconi, E. Corbelli, L. Tomasso, L. Querques, G. Zerbini, et al., Optical coherence tomography angiography analysis of retinal vascular plexuses and choriocapillaris in patients with type 1 diabetes without diabetic retinopathy, Acta Diabetol. 54 (7) (juill 2017) 695–702.

[28] H. Lee, M. Lee, H. Chung, H.C. Kim, Quantification OF retinal vessel tortuosity IN diabetic retinopathy using optical coherence tomography angiography, Retina 38 (5) (Mai 2018) 976–985.

[29] W.A. Samara, A. Shahlaee, M.K. Adam, M.A. Khan, A. Chiang, J.I. Maguire, et al., Quantification of diabetic macular ischemia using optical coherence tomography angiography and its relationship with visual acuity, Ophthalmology 124 (2) (2017) 235–244.

[30] T.S. Hwang, S.S. Gao, L. Liu, A.K. Lauer, S.T. Bailey, C.J. Flaxel, et al., Automated quantification of capillary nonperfusion using optical coherence tomography angiography in diabetic retinopathy, JAMA Ophthalmol 134 (4) (avr 2016) 367–373.

[31] H.R. AttaAllah, A.A.M. Mohamed, M.A. Ali, Macular vessels density in diabetic retinopathy: quantitative assessment using optical coherence tomography angiography, Int. Ophthalmol. 39 (8) (août 2019) 1845–1859.

[32] G. Dimitrova, E. Chihara, H. Takahashi, H. Amano, K. Okazaki, Quantitative retinal optical coherence tomography angiography in patients with diabetes without diabetic retinopathy, Invest. Ophthalmol. Vis. Sci. 58 (1) (01 2017) 190–196.

[33] G.H. Bresnick, R. Condit, S. Syrjala, M. Palta, A. Groo, K. Korth, Abnormalities of the foveal avascular zone in diabetic retinopathy, Arch. Ophthalmol. 102 (9) (Sept 1984) 1286–1293.

[34] T. Hamanaka, N. Akabane, T. Yajima, T. Takahashi, A. Tanabe, Retinal ischemia and angle neovascularization in proliferative diabetic retinopathy, Am. J. Ophthalmol. 132 (5) (Nov 2001) 648–658.

[35] R.F. Spaide, J.M. Klancnik, M.J. Cooney, Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography, JAMA Ophthalmol 133 (1) (janv 2015) 45–50.

[36] F.J. Freiberg, M. Pfau, J. Wons, M.A. Wirth, M.D. Becker, S. Michels, Optical coherence tomography angiography of the foveal avascular zone in diabetic retinopathy, Graefes Arch. Clin. Exp. Ophthalmol. 254 (6) (juin 2016) 1051–1058.

[37] C. Balaratnasingam, M. Inoue, S. Ahn, J. McCann, E. Dhrami-Gavazi, L. A. Yannuzzi, et al., Visual acuity is correlated with the area of the foveal avascular zone in diabetic retinopathy and retinal vein occlusion, Ophthalmology 123 (11) (2016) 2352–2367.

[38] M.C. Savastano, M. Federici, B. Falsini, A. Caporossi, A.M. Minnella, Detecting papillary neovascularization in proliferative diabetic retinopathy using optical coherence tomography angiography, Acta Ophthalmol. 96 (3) (mai 2018) 321–323.

[39] J. Conrath, R. Giorgi, D. Raccah, B. Ridings, Foveal avascular zone in diabetic retinopathy: quantitative vs qualitative assessment, Eye 19 (3) (Mars 2005) 322–326.

[40] W.A. Samara, E.A.T. Say, C.T.L. Khoo, T.P. Higgins, G. Magrath, S. Ferenczy, et al., Correlation OF foveal avascular zone size with foveal morphology IN normal eyes using optical coherence tomography angiography, Retina 35 (11) (Nov 2015) 2188–2195.

[41] N. Takase, M. Nozaki, A. Kato, H. Ozeki, M. Yoshida, Y. Ogura, Enlargement OF foveal avascular zone IN diabetic eyes evaluated BY en face optical coherence tomography angiography, Retina 35 (11) (nov 2015) 2377–2383.

[42] A. Shahlaee, M. Pefkianaki, J. Hsu, A.C. Ho, Measurement of foveal avascular zone dimensions and its reliability in healthy eyes using optical coherence tomography angiography, Am. J. Ophthalmol. 161 (janv 2016) 50–55.e1.

[43] A.M. Mansour, A. Schachat, G. Bodiford, R. Haymond, Foveal avascular zone in diabetes mellitus, Retina 13 (2) (1993) 125–128.

[44] J.M. Provis, A.E. Hendrickson, The foveal avascular region of developing human retina, Arch. Ophthalmol. 126 (4) (avr 2008) 507–511.

[45] K. Sambhav, K.K. Abu-Amero, K.V. Chalam, Deep capillary macular perfusion indices obtained with OCT angiography correlate with degree of nonproliferative diabetic retinopathy, Eur. J. Ophthalmol. 27 (6) (8 nov 2017) 716–729.

[46] T.E. de Carlo, M.A. Bonini Filho, C.R. Baumal, E. Reichel, A. Rogers, A.J. Witkin, et al., Evaluation of preretinal neovascularization in proliferative diabetic retinopathy using optical coherence tomography angiography, Ophthalmic Surg Lasers Imaging Retina 47 (2) (févr 2016) 115–119.

[47] G. Di, Y. Weihong, Z. Xiao, Y. Zhikun, Z. Xuan, Q. Yi, et al., A morphological study of the foveal avascular zone in patients with diabetes mellitus using optical coherence tomography angiography, Graefes Arch. Clin. Exp. Ophthalmol. 254 (5) (Mai 2016) 873–879.

[48] J. Gozlan, P. Ingrand, O. Lichtwitz, A. Cazet-Supervielle, L. Benoudis, M. Boissonnot, et al., Retinal microvascular alterations related to diabetes assessed by optical coherence tomography angiography: a cross-sectional analysis, Medicine (Baltim.) 96 (15) (avr 2017) e6427.

[49] Classification of diabetic retinopathy from fluorescein angiograms. ETDRS report number 11. Early treatment diabetic retinopathy study research group, Ophthalmology 98 (5 Suppl) (mai 1991) 807–822.

[50] V. Mané, B. Dupas, A. Gaudric, S. Bonnin, A. Pedinielli, E. Bousquet, et al., Correlation between cystoid spaces IN chronic diabetic macular edema and capillary nonperfusion detected BY optical coherence tomography angiography. Retina (philadelphia, Pa), déc 36 (Suppl 1) (2016) S102–S110.

[51] F.Y. Tang, D.S. Ng, A. Lam, F. Luk, R. Wong, C. Chan, et al., Determinants of quantitative optical coherence tomography angiography metrics in patients with diabetes, Sci. Rep. 7 (1) (31 2017) 25–75.