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Nailfold capillaroscopy in diabetes mellitus

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ABSTRACT

Introduction: Diabetes mellitus (DM) is characterized by chronic hyperglycemia states and the development of specific microvascular disorders such as retinopathy and nephropathy. Conventional methods are used to study the vascular compromise of this entity, however, the use of capillaroscopy for the evaluation of capillary microarchitecture is not frequently used.

Methods and materials: Observational and descriptive study of 65 patients with an established diagnosis of DM and a control group that underwent an initial capillaroscopy examination. The parameters considered were: Capillary diameter (ectasia and giant capillaries), cross-linked, tortuous, arborified capillaries, avascular zones, haemorrhages, dominant morphology, visibility of the subpapillary venous plexus (SPVP), cuticulitis and SD pattern.

Results: Capillaroscopy was performed in 65 patients, the findings were: tortous capillaries (63%), crosslinked capillaries (59%), avascular areas (48%), ectasias (39%), giant capillaries (11%). The capillaroscopic findings were evident in the majority of the studied population, 83%, compared to 17% who did not have capillaroscopic alterations.

Conclusion: Significant capillaroscopic changes were demonstrated in patients with DM, in turn, we described a specific pattern consisting of: capillary dilatation, avascular zones and tortuous capillaries. Patients with more comorbidities and evolution of the disease showed greater microvascular damage.

1. Introduction

Diabetes is characterized by a chronic hyperglycemic state and the development of alterations in the vascular structure. It's currently considered a chronic disease with a high mortality rate due to its longterm cardiovascular and renal complications (Cowie et al., 2009; American Diabetes Association, 2016).

The worldwide prevalence varies from 3.8–10.2% and the rate of non-diagnosed cases is 50%, making it a major global health problem (McCulloch, 2016).

The evaluation of these patients has been managed by a group of experts, and management guidelines (American Diabetes Association, 2016). The importance of these guidelines lies in the multidisciplinary management of diabetic patients, highlighting the usefulness of screening techniques for the detection of a systemic compromise, making it a referral source for both primary care physicians and specialists (McCulloch, 2016).

Data from the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) shows that chronic hyperglycemia is the most important risk factor for the development of microvascular complications in patients with type I and II diabetes mellitus (The Diabetes Control and Complication Trial Research Group, 1993; UK Prospective Diabetes Study (UKPDS) Group, 1998) and that endothelial dysfunction plays an important role in the development of vascular diseases and represents the initial stage in pathogenesis of the disease (Shestakova et al., 2005). The current trend for evaluating microvascular damage in diabetic patients is the use of: Doppler flowmetry, direct and indirect ophthalmoscopy, ambulatory blood pressure monitoring (Hosking et al., 2013), but capillaroscopy is not commonly used.

Because of diabetes important vascular involvement, direct observation tools such as ophthalmoscopes, and magnifying lenses have been used during examination. In recent years, capillaroscopy has gained recognition in the field of diseases that affect capillary microarchitecture, especially in rheumatic diseases (do Rosário e Souza and Kayser, 2015); however, studies published in the last decade highlight the importance of this innovative technique in non-rheumatic diseases such as diabetes (Romano et al., 2015; Rajaei et al., 2015; Kuryliszyn-Moska et al., 2011). These studies conclude that capillaroscopy provides important data for the determination of vascular damage in diabetic patients,

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allowing an evaluation in the progression of the disease (Barchetta et al., 2011; Lin et al., 2009; Kuryliszyn-Moskal et al., 2006).

The purpose of this study was to identify vascular alterations in patients with type II diabetes mellitus and to determine the relationship between capillaroscopic findings and diabetic complications.

2. Methods

A descriptive observational study on patients with established diagnosis of diabetes mellitus II using inclusion and exclusion criteria.

2.1. Inclusion criteria

The participants in this study had to meet the following inclusion criteria:

- Established diagnosis of Type II Diabetes Mellitus according to the criteria of the American Diabetes Association (ADA) (American Diabetes Association, 2016).
- Age group 20–70 years.

2.2. Exclusion criteria

- Preexisting disease that affects the vascular architecture.
- Patients with trauma in the periungual fold of the fourth and fifth fingers of the non-dominant hand.
- Patients with aesthetic treatments at the nail (enamel and acrylic), in the last two weeks prior to the study.

In addition, a selection of a control group was performed, which had to meet the following inclusion criteria: age group 20–70 years and no previous medical history of Diabetes Mellitus, connective tissue diseases or Raynaud's phenomenon.

All of the studied population had a videocapillaroscopy performed in the nailfold of the fourth and fifth fingers of the non-dominant hand and the data was recorded in a previously established data file.

2.3. Capillaroscopy technique

Capillaroscopy was performed by an experienced Rheumatologist in a room with an ambient temperature of 20–23 °C. The fourth and fifth finger of the non-dominant hand was chosen as a homogeneous method and reference from the studies carried out by Lin et al. (Lin et al., 2009); with hands placed at a heart level and in a seated position.

For the examination of each finger, a drop of immersion oil was placed in the nailfold to improve visibility. The capillaries were observed with a 100× magnification capillaroscope (Dino-Lite) and photographs were taken of the last distal row of the capillaries. The procedure lasted approximately 15 min for each subject. The images were analyzed using the software DinoXcope version 1.15, in which measurements of the capillaries were made and the characteristics of the capillary micro-architecture were carefully visualized.

The following capillaroscopic parameters were taken into account: Capillary diameters (ectasias and giant capillaries), cross-linked capillary, tortuous, arborified, avascular areas, haemorrhages, dominant morphology, visibility of the subpapillary venous plexus (SPVP), cuticulitis and SD pattern.

2.4. Capillaroscopic parameters

The alterations were described as follows:

- Capillary diameter: according to Maricq descriptions the normal range is 25–50 μm. Ectasias are capillaries with arterial or venous branches that measure >15–20 μm (Maricq, 1981), and giant capillaries are those that surpass the normal range of 4–10 times the width of the apical loop (Hou et al., 2012; Lefford and Edwards, 1986; Hofstee et al., 2012) and the determination of a capillary mean that is the result of an average of 3 measurements (Cutolo et al., 2005; Grassi and Del Medico, 2004).
- Cross-linked capillaries: similar to branches that intersect like a number eight and tortuous like capillaries with branches in an undulating, sinuous or twisted arrangement (Cutolo et al., 2005; Grassi and Del Medico, 2004).
- Ramified capillaries: they were described as those capillaries that adopt the shape similar to a tree (Grassi and Del Medico, 2004).
- Avascular zones: they were defined as the absence of capillaries in a tract superior to 500 μm (Grassi and Del Medico, 2004).
- Haemorrhages: as the hemosiderin deposit, caused by the rupture of one or more capillaries (Maricq, 1981).
- Dominant morphology: finding that predominates in >20%, whether it's open, tortuous or cross-linked (Restrepo et al., 2008; Ríos et al., 2016).
- Visibility of the subpapillary venous plexus: a network of larger vessels with respect to the capillaries. The presence of the parameter was determined according to the Kabasakal and Col. by (Kabasakal et al., 1996):
- 0: not visible.
- 1: doubtful or limited visibility.
- 2: Plexus visible in certain areas.
- 3: Fully visible in large areas
- Cuticulitis: inflammation of the insertion of the cuticle at the periungual fold (Andrade et al., 1999).
- SD pattern: presence of: giant capillaries, avascular zones, haemorrhages and ramified capillaries all together (Maricq, 1981).

In addition, indirect ophthalmoscopy was performed using a technique validated by Kim D. et al. A 20D magnification lens and a smartphone were used to capture the images (Kim et al., 2012; Haddock et al., 2013; Chhablani et al., 2012). For the interpretation and classification of eye involvement, we used the guidelines of the Pacific Eye Institute, New Zealand – 2010 (Pacific Eye Institute, 2010) which is focused on primary care physicians, health coordinators and allied health personnel. These guidelines maintain the classification of the World Health Organization (WHO) (WHO, 2006) and the American Academy of Ophthalmology (AAO) (American Academy of Ophtalmology, 2016; American Academy of Ophtalmology, 2008).

3. Statistics analysis

Data was analyzed using SPSS version 22 software. Non-parametric correlations were performed using Kendall's tau_b and values of $p \leq 0.05$ and two tails were considered statistically significant.

4. Results

We studied 65 patients, with a mean age of 57 ± 8.94 [39–80] years. 75% [49] were women and 25% (Hou et al., 2012) men. Regarding their demographic data (Table 1), 99% [64] of the patients studied were Ecuadorian-Hispanics, compared to 1% (Cowie et al., 2009) of Latin-African Americans.

About comorbidities, 65% [42] suffered from hypertension, 15% (Rajaei et al., 2015) hypothyroidism, 8% (American Diabetes Association, 2016) gastritis, 3% (American Diabetes Association, 2016) allergies (rhinitis), no evidence of neoplasias. Using their body mass index (BMI), 35% (Kabasakal et al., 1996) were found overweight, 32% (Restrepo et al., 2008) ideal weight, 26% (Lefford and Edwards, 1986) obesity and 6% (The Diabetes Control and Complication Trial Research Group, 1993) underweight. Smoking habit was seen in 8% (UK Prospective Diabetes Study (UKPDS) Group, 1998) of the population studied, considering smoking, to the tobacco consumption of at least 1 cigarette per day for at least 6 months (Pacific Eye Institute, 2010). As for metabolic markers, mean abdominal circumference was 98.32 ±

Table 1
Demographic data.

Parameters	n	%	Control group n = 50		p < 0.05
			n	%	
Sex					
Women	49	75	36	72	–
Men	16	25	14	28	–
Mean age	57 ± 8.94		49	[27–68]	–
Ethnicity					
Ecuadorian-Hispanics	64	99	40	60	–
Latin-African Americans	1	1	10	20	–
Marital status					
Single	10	15	5	10	–
Married	33	51	43	86	–
Cohabitation	22	17	1	2	–
Divorced	3	5	1	2	–
Widower	8	12	–	–	–
Evolution of disease					
Years mean	12 ± [12–40]				–

Table 3
Frequency of capillaroscopic findings.

Capillaroscopic findings	n	%	Control Group n = 50		p < 0.05
			n	%	
Tortous capillaries	41	63	10	20	0.008
Cross-linked capillaries	38	59	26	52	–
Avascular zones	34	48	2	4	0.000
Ectasias	25	39	15	30	–
Cuticulitis	20	31	9	18	0.03
Giant capillaries	9	14	6	12	0.07
Ramified capillaries	7	11	2	4	0.02
SPVP visibility	5	8	13	26	–
Haemorrhage	0	0	0	0	–
SD pattern	0	0	0	0	–
Open morphology	19	30	41	82	–
Cross-linked morphology	16	25	3	6	–
Tortuous morphology	29	45	5	12	–

17.93 cm, systolic blood pressure 131 ± 17.62 mm Hg, diastolic 75 ± 10.42 mm Hg and blood glucose 167 mg/dL. The most frequent comorbidity was diabetic neuropathy 77% [50] (Table 2).

The capillaroscopic findings (Table 3) were evident in the majority of the studied population, 83% [54], compared to 17% (Kuryliszyn-Moska et al., 2011) who did not have capillaroscopic alterations (Fig. 1).

The most frequent alterations were tortuous capillaries in 63% [41], capillary cross-linking 59% (Bollinger and Fagrell, 1990), avascular areas 48% (Chang et al., 1997), ectasias 31% (Kim et al., 2012). Other alterations found were giant capillaries 14% (Romano et al., 2015), ramified capillaries 11 (Hosking et al., 2013). No haemorrhages, nor SD pattern were found. The mean number of alterations was 2 [0–6], showing that within this group each individual had at least two capillaroscopic alterations (Table 3).

Table 2
Comorbidities, habits and diabetic complications.

Parameters	n	%	Control group n = 50		p < 0.05
			n	%	
Comorbidities					
Gastritis	5	7	7	14	–
Allergies (rhinitis)	2	3	10	20	0.003
Hypertension	42	65	3	6	0.040
Hypothyroidism	10	15	–	–	0.033
Neoplasias	–	–	–	–	–
Body mass index					
Underweight	4	6	2	4	–
Ideal weight	21	32	30	60	–
Overweight	23	35	13	26	–
Obesity	17	26	5	10	–
Habits					
Drugs	–	–	2	4	–
Alcohol	–	–	13	27	–
Smoking	6	8	8	16	0.003
Metabolic markers					
Mean abdominal circumference			98.32 ± 17.93		–
Blood pressure					–
Systolic			131 ± 17.62 mm Hg		
Diastolic			75 ± 10.42 mm Hg		
Blood glucose			167 ± 78.43		

Diabetic complications	n	%	
Diabetic neuropathy	50	77	0.004
Urinary tract infection	24	37	–
Peripheral vascular disease	16	25	0.000
Diabetic sclerosis	12	19	0.01
Retinopathy	12	19	0.001
Hypoacusia	11	17	–
Nephropathy	8	12	0.001
Arteriopathy	6	9	0.03
Cerebral vascular disease	4	6	–
Diabetic ulcers	4	6	0.000
Periodontal disease	3	5	–
Gastroparesia/diarrhea	1	2	–

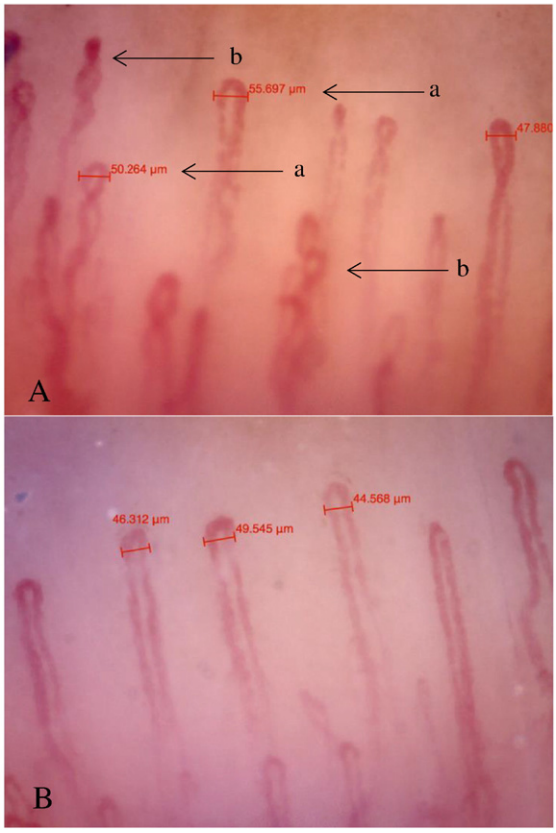

Fig. 1. Example of capillaroscopic alterations in a diabetic patient and a healthy subject. A. capillary dilation b. Capillaries, cross-linked and tortuous, B. Normal capillaroscopy, homogeneous arrangement of the capillaries of the last distal row, diameters within normal parameters.

The arrangement of the capillaries in the nailfold was observed in a tortuous pattern or morphology in 45% (WHO, 2006), open 30% (Cutolo et al., 2005), cross-linked 25% (Hou et al., 2012), with a mean capillary diameter of approximately 43.14 ± 5.72 μm which is within the normal parameters. When compared against the control group, patients with diabetes mellitus presented greater capillary diameter.

The capillaroscopic findings representing vascular damage were greater in patients with diabetes mellitus than in the control group. Avascular zones, tortuous and arborified capillaries were more frequent in patients with DM. The capillary morphology in the control group was open versus tortuous in patients with DM.

Patients with capillaroscopic alterations had a longer time of evolution of the disease with an average of 12.8 years, compared to those who did not present alterations that had a mean evolution of the disease of 8.5 years, which shows that capillaroscopic alterations represent progressive endothelial damage.

Approximately 63% [41] of the study population had high glycemia levels >110 mg/dL, from which 100% [41] presented tortuous capillaries, 93% (Bollinger and Fagrell, 1990) cross-linked capillaries, 49% (Grassi and Del Medico, 2004) cuticulitis (95% CI 0.19–0.82), 22% (Romano et al., 2015) giant capillaries (CI 95% 0.09–0.48), 17% (Hosking et al., 2013) arborified capillaries (95% CI 0.07–0.40), and 12% (UK Prospective Diabetes Study (UKPDS) Group, 1998) visibility of the subpapillary venous plexus (IC 85% 0.04–0.32) (Fig. 2).

Among the normoglycemic group [$n = 24$], 71% (Lefford and Edwards, 1986) presented tortous capillaries, 75% (Hofstee et al., 2012) cross-linked capillaries, 29% (Hosking et al., 2013) cuticulitis, 13% (McCulloch, 2016) avascular areas, 8% 13% (McCulloch, 2016) and 8% (American Diabetes Association, 2016) visibility of the subpapillary venous plexus (Fig. 2).

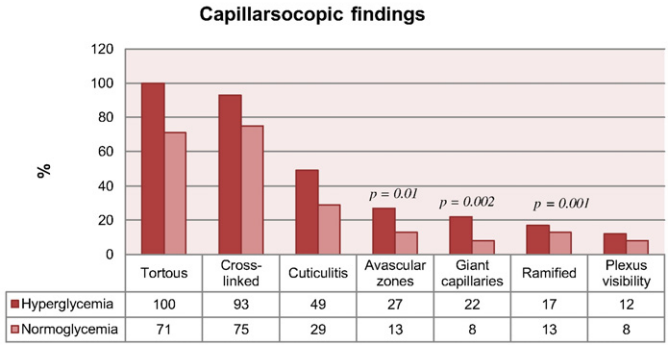

Fig. 2. Capillaroscopic findings in hyperglycemic patients and normoglycemic patients.

Capillaroscopic alterations were analyzed, and an association between the presence of retinopathy and capillary damage at the level of the nailfold was demonstrated (Table 4) (Fig. 3).

5. Discussion

Nailfold capillaroscopy is a noninvasive method for the observation of the capillary microvasculature. This study demonstrated that the use of capillaroscopy in patients with diabetes allows the identification of capillaroscopic abnormalities, possibly including a characteristic pattern in this group of patients consisting of tortuous, cross-linked capillaries, avascular zones and ectasias. It was found that most of the diabetic patients presented these abnormalities, as opposed to the control group.

Kuryliszyn-Moskal et al. studied microvascular changes by capillaroscopy in patients with type I diabetes mellitus and the association with systemic compromise, the impact of disease duration, and metabolic control on changes in capillary architecture. They found that patients with type I diabetes mellitus had important capillary changes such as tortuosities, dilated capillaries, and a reduction in capillary density compared to the control group in which capillaroscopic abnormalities were not found. Patients with signs of systemic involvement had moderate-severe capillary changes, and patients with poor metabolic

Table 4
Capillaroscopic findings in patients with minimal/simple and pre-proliferative diabetic retinopathy.

Capillaroscopic findings	R1 minimum/simple		$p < 0.05$
	$n = 5$	%	
Avascular zones	1	20	0.000
Ectasias	2	40	0.000
Haemorrhages	–	–	–
Giant capillaries	–	–	–
Tortous capillaries	2	40	0.000
Ramified capillaries	–	–	–
Cuticulitis	2	40	0.000
Cross-linked capillaries	1	20	0.03
Subpapillary venous plexus	1	20	0.024
Average capillary diameter	42.58 ± 2.09 μm		–
Capillaroscopic findings	R2 pre-proliferative		$p < 0.05$
	$n = 7$	%	
Avascular zones	6	86	0.000
Ectasias	3	43	0.000
Haemorrhages	–	–	–
Giant capillaries	2	29	0.002
Tortous capillaries	7	100	0.000
Ramified capillaries	3	43	0.001
Cuticulitis	7	100	0.000
Cross-linked capillaries	5	71	0.04
Subpapillary venous plexus	2	29	0.024
Average capillary diameter	49.84 ± 5.24 μm		–

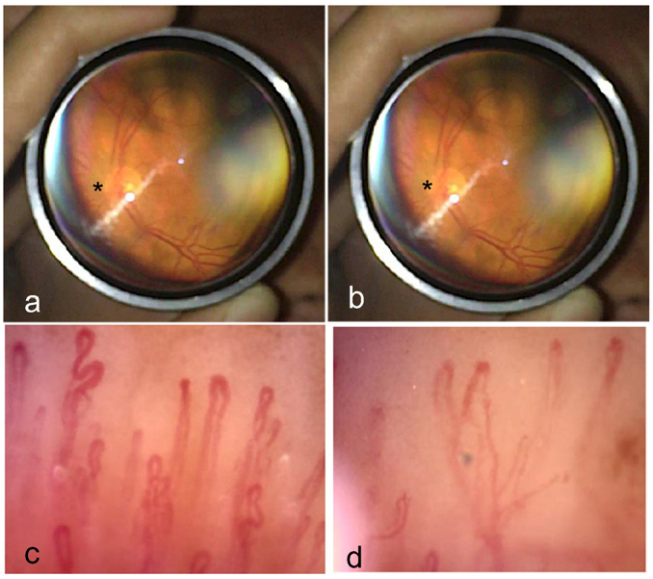

Fig. 3. A–B: Eye Fundoscopy – Minimum/simple retinopathy R1 in diabetic patient. C–D: Capillaroscopy of a diabetic patient: altered vascular structure characterized by tortuous capillaries, cross-linked, ramified, ectasias and a slight decrease in capillary density. (*) Microaneurysms, R1: ≤ 5 microaneurysms and/or haemorrhagic dots.

control demonstrated severe capillaroscopic changes (Kuryliszyn-Moskal et al., 2006).

Meyer et al. studied the morphological changes at periungual nailfold level in patients with diabetes, and demonstrated that there are capillaroscopic alterations such as increased capillary diameter, tortuosities and decreased capillary density. These findings were shown to be associated with vascular reactivity generated by ischemia (Meyer et al., 2011).

Pazos-Moura evaluated capillary morphology and density by capillaroscopy in patients with type I and II diabetes mellitus. The main capillaroscopic alterations found were tortuosities, increase in capillary diameter and decrease in capillary density. The study showed that patients with type II diabetes had more alterations capillaroscopic findings than patients with type I diabetes mellitus and that there is an association between capillary findings and metabolic control (Pazos-Moura et al., 1987).

Romano et al. In their most recent editorial highlight the advantages of using capillaroscopy in patients with diabetes, because it is a non-invasive method that allows physicians to evaluate the morphological parameters of the capillary microarchitecture and to be a predictor of the extent, severity and evolution of the disease. Capillaroscopy being a dual tool for the diagnosis and prognosis of diabetic microangiopathy, is indicated for all pathologies whose pathogenesis compromises anatomical and functional abnormalities of the microcirculation (Romano et al., 2015).

Hosking et al. used capillaroscopy as a non-invasive technique for the detection of microvascular changes in the pediatric population and adolescents with type I diabetes mellitus. The most frequent alterations found were avascular zones and microhaemorrhages. Avascular zones were associated in patients with diabetic complications ($p = 0.03$) and microhaemorrhages were associated with elevated HbA1c levels ($p = 0.03$), concluding that capillaroscopy is a method that can easily detect microvascular damage (Hosking et al., 2013).

Kuryliszyn-Moskal et al. demonstrated that microvascular involvement is one of the main causes of diabetic complications. They used capillaroscopy as a study tool for capillary micro-architecture in patients with type I diabetes mellitus and found an association between complications and serum levels of IL-18 and Selectin-sE. Severe capillaroscopic changes were found in the group of patients with microangiopathic complications and elevated levels of inflammatory markers (Kuryliszyn-Moska et al., 2011).

Our results were similar to those shown by Meyer et al., who observed tortuous, dilated capillaries and normal capillary density in patients with diabetes mellitus type I and II when compared against a control group (Meyer et al., 2011). Similar data was published by Chang, where tortuous capillaries and increased capillary diameter were the most relevant alterations within the group of patients with DM (Chang et al., 1997).

Rajaei et al. studied the capillaroscopic changes in patients with diabetes mellitus and demonstrated that ramified and tortuous capillaries were more frequent in these patients, compared to a control group (Rajaei et al., 2015). Kaminska-Winciorek et al. identified an increase in cross-linked capillaries, results that are similar to the ones found in our study (Kaminska-Winciorek et al., 2012). Cicco et al. showed a decrease in total capillary density by 28%(Cicco and Cicco, 2007), a higher result compared to our total value of 11%, however, we can attribute this difference to the size of the population studied.

A study carried out by the authors showed that approximately 86% of the healthy subjects that were studied had capillary findings such as tortuous, cross-linked and ramified capillaries (Ríos et al., 2016). These results are similar to the study by Hoerth (Hoerth et al., 2012) in which it was shown that 85% of the subjects had capillaroscopic findings such as: tortuous, cross-linked and ramified capillaries. Coehlo Andrade studied a more extensive cohort and approximately 81% of the subjects presented capillary findings including ramified and tortuous capillaries (Bollinger and Fagrell, 1990). This supports the capillaroscopic alterations that we evidenced in the control group.

Barchetta studied the possible relationship of microangiopathic lesions detected in retinal vessels and capillary changes in patients with type I and type II diabetes (Barchetta et al., 2011). He observed that diabetic patients had greater capillary diameter, vascular ectasias and peringueal edema in comparison with healthy subjects. Patients with type 1 DM had more capillaroscopic alterations than patients with type II DM. Also, capillaroscopy was able to identify alterations in almost 50% of patients with DM without retinopathy, revealing an early microangiopathic alteration (Barchetta et al., 2011).

It is important to emphasize on the time of disease evolution and the appearance of capillaroscopic alterations. Our study shows that patients with greater time of disease evolution had more capillaroscopic alterations than those with less evolution time. Kuryliszyn et al. showed a progressive appearance of ramified capillaries in diabetic patients with a prolonged evolution time (>10 years) (Kuryliszyn-Moskal et al., 2006). Similar data was shown in the study by Bollinger et al. where they found more capillaroscopic alterations in those patients with a time of disease evolution >10 years (Bollinger and Fagrell, 1990).

These results highlight the importance of evaluating the progression of vascular damage in this group of patients that begins with a loss of capillary density compensated by the appearance of ramifications and capillary dilatation which in turn contributes to the pathogenesis of complications in the disease.

In our study we found that ocular compromise was present in 18% of the diabetic patients when comparing capillary findings and indirect ophthalmoscopy. We found an association between microangiopathies and the presence of ramified capillaries and avascular zones, similar to the study by Chang et al. where they found a correlation between diabetic retinopathy and the presence of tortuous, ramified capillaries and capillary dilatation, in addition to confirming that these alterations are increased with the severity of diabetic retinopathy (Chang et al., 1997), however our sample is limited and further research is needed focused on these two tools, because of the relationship and detection of vascular damage with them is evident.

The main advantage and strength of this study was to demonstrate the capacity of the capillaroscopy to identify diabetic microangiopathy, in addition to being the first study in Ecuador with this approach. The results found were similar to other international publications. Our

main limitation was not having recorded enough clinical data such as laboratory tests (HbA1c levels, lipid profile, etc.) to be able to analyze a relationship with the capillaroscopic alterations; in addition to the limited number of patients.

6. Conclusions

Capillaroscopy has proved to be a non-invasive, reproducible and reliable technique for the evaluation of vascular microarchitecture within a large group of rheumatic diseases such as scleroderma, polymyositis, dermatomyositis, mixed connective tissue disease, and others (Hofstee et al., 2012). This study performed on diabetes patients and cannot be generalized for the evaluation of other diseases.

Conflict of interest

Authors declare no conflict of interest.

References

American Academy of Ophtalmology, 2008. Diabetic Retinopathy Preferred Practice Pattern. Am Acad Ophtalmol.

American Academy of Ophtalmology, 2016. Diabetic Retinopathy Preferred Practice Pattern [Updated 2016]. Am Acad Ophtalmol.

American Diabetes Association, 2016. Standards of medical care in diabetes. Diabetes Care 39 (1), S13–S23.

Andrade, L., Gabriel, A., Assad, R., Ferrari, A., Atra, E., 1999. Panoramic nailfold capillaroscopy: a new reading method and normal range. Semin. Arthritis Rheum. 20 (1), 21–31.

Barchetta, I., Riccieri, V., Vasile, M., Stefanantoni, K., Comberiati, P., Taverniti, L., et al., 2011. High prevalence of capillary abnormalities in patients with diabetes and association with retinopathy. Diabet. Med. 28 (9), 1039–1044.

Bollinger, A., Fagrell, B., 1990. Clinical Capillaroscopy - A Guide to Its Use in Clinical Research and Practice. Hogrefe & Huber Publishers, Toronto, pp. 1–123.

Chang, C.H., Tsai, R.K., Wu, W.C., Kuo, S.L., Yu, H.S., 1997 Mar. Use of dynamic capillaroscopy for studying cutaneous microcirculation in patients with diabetes mellitus. Microvasc. Res. 53 (2), 121–127.

Chhablani, J., Kaja, S., Shah, V., 2012. Smartphones in ophtalmology. Indian J. Ophthalmol. 60 (2), 127–131.

Cicco, G., Cicco, S., 2007. Hemorheology and microcirculation in some pathologies of internal medicine. Minerva Med. 98, 625–631.

Cowie, C., Rust, K., Ford, E., Eberhardt, M., Byrd-Hlot, D., Li, C., et al., 2009. Screening for type 2 diabetes mellitus. Diabetes Care 32 (2), 287.

Cutolo, M., Pizzorni, C., Sulli, A., 2005. Capillaroscopy. Best Pr. Res. Clin. Rheumatol. 3, 437–452.

do Rosário e Souza, E., Kayser, C., 2015. Nailfold capillaroscopy: relevance to the practice of rheumatology. Rev. Bras. Reumatol.

Grassi, W., Del Medico, P., 2004. Atlas of Capillaroscopy. Edra Medical Publishing & New Media, Milan.

Haddock, L., Kim, D., Mukai, S., 2013. Simple, inexpensive technique for high-quality smartphone fundus photography in human and animal eyes. J. Ophthalmol. 518479, 5.

Hoerth, C., Kundi, M., Katzenschlager, R., Hirschl, M., 2012. Qualitative and quantitative assessment of nailfold capillaries by capillaroscopy in healthy volunteers. Vasa. Vasa. 41, 19–26.

Hofstee, H., Serné, E., Roberts, C., 2012. A multicentre study on the reliability of qualitative and quantitative nail-fold videocapillaroscopy assessment. Rheumatology 51 (4), 749–755.

Hosking, S., Bhatia, R., Crock, P., Wright, I., Squance, M., Reeves, G., 2013. Non-invasive detection of microvascular changes in a paediatric and adolescent population with type 1 diabetes: a pilot cross-sectional study. BMC Endocr. Disord. 13 (41).

Hou, M., Huang, S., Wang, H., Tseng, C., Lo, L., Chen, Y., 2012. A computerized system of nail-fold capillaroscopy for dry eye disease diagnosis. Multidim. Syst. Sign. Process. 23 (4), 512–524.

Kabasakal, Y., Elvins, D., Ring, E., McHugh, N., 1996. Quantitative nailfold capillaroscopy findings in a population with connective tissue disease and in normal healthy controls. Ann. Rheum. Dis. 55 (507), 12.

Kaminska-Winciorek, G., Deja, G., Polańska, J., Jarosz-Chobot, P., 2012. Diabetic microangiopathy in capillaroscopic examination of juveniles with diabetes type 1. Postepy Hig. Med. Dosw. 66, 51–59.

Kim, D., Delori, F., Mukai, S., 2012. Smartphone photgraphy safety. Ophthalmology 119 (10), 2200–2201.

Kuryliszyn-Moska, A., Dubicki, A., Zarzycki, W., Zonnenberg, A., Górska, M., 2011. Microvascular abnormalities in capillaroscopy correlate with higher serum IL-18 and sE-selectin levels in patients with type 1 diabetes complicated by microangiopathy. Folia Histochem. Cytobiol. 49, 104–110.

Kuryliszyn-Moskal, A., Dubicki, A., Zaezycki, W., Zonnenberg, A., Gorska, M., 2006. A study on microvascular abnormalities in capillaroscopy in patients with type 1 diabetes mellitus. Diabetol Dosw i Klin. 6 (2), 98–103.

Lefford, F., Edwards, J., 1986. Nailfold capillary microscopy in connective tissue disease: quantitative morphological analysis. Ann. Rheum. Dis. 45, 741–749.

Lin, K., Cheng, T., Chen, C., 2009. Clinical applications of nailfold capillaroscopy in different rheumatic diseases. J. Int. Med. Taiwan 20, 238–247.

Maricq, H., 1981. Widefield capillary microscopy technique and rating scale for abnormalities seen in scleroderma and related disorders. Arthritis Rheum. 9, 1159–1165.

McCulloch, D., 2016. Screening for type 2 diabetes mellitus. UptoDate.

Meyer, M., Pfhol, M., Schatz, H., 2011. Asssesment of diabetic alterations of microcirculation by means of capillaroscopy and laser-Doppler anemometry. Med. Klin. 15, 71–77.

Pacific Eye Institute, 2010. Diabetes Retinal Screening, Grading and Management Guidelines for Use in Pacific Island Nations, 2010. Diabetes Work Group, Fred Hollows Found Pacific Eye Institute, Auckland, New Zeal.

Pazos-Moura, C., Moura, E., Bouskela, E., Torres-Filho, I., Breitenbach, M., 1987. Nailfold capillaroscopy in diabetes mellitus morphological abnormalities and relationship with microangiopathy. Braz. J. Med. Biol. Res. 20, 777–780.

Rajaei, A., Dehghan, P., Farahani, Z., 2015. Nailfold capillaroscopy findings in diabetic patients (a pilot cross-sectional study). Open J Pathol. 5, 65–72.

Restrepo, J.P., Gutiérrez, M., De Angelis, R., Grassi, W., 2008. El papel de la capilaroscopia del lecho ungueal en reumatología. Rev. Colomb. Reumatol. 15 (3), 187–195.

Ríos, C., Maldonado, G., Ferro, C., Ríos, K., 2016. Estudio de patrones capilaroscópicos en población sana. Rev. Arg. Reum. 27 (1), 27–31.

Romano, C., Costa, M., Messina, M., Bertini, M., 2015. Videocapillaroscopy in Diabetes. Diabetes Res. Open J. 2 (3), 3–6.

Shestakova, M., Jarek-Martynowa, I., Ivanishina, N., 2005. Role of endothelial dysfunction in the development of cardiorenal syndrome in patients with type 1 diabetes mellitus. Diabetes Res. Clin. Pract. 68 (1), 65–72.

The Diabetes Control and Complication Trial Research Group, 1993,. The effect of intensive treatment of diabetes in the devel- opment and progression of long-term complications in insulin dependent diabetes mellitus. N. Engl. J. Med. 329, 977–986.

UK Prospective Diabetes Study (UKPDS) Group, 1998. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 352, 837–853.

WHO, 2006. Prevention of Blindness from Diabetes Mellitus. Geneva, Switz.