Diabetic retinopathy and subclinical retinal microvascular and neurosensory changes in military personnel with type 2 diabetes: a retrospective and prospective optical coherence tomography angiography study

A. K. Matkarimov[1], F. A. Bakhritdinova[2]

[1]*Military Medical Institute of the University of Military Security and Defense of the Republic of Uzbekistan*

[2]*Department of Ophthalmology, Tashkent Medical Academy, Tashkent, Uzbekistan*

Published 30 September 2026 | DOI: 10.14419/j.jtumed.2026.09.30

Abstract

Objective. To determine the frequency of diabetic retinopathy (DR) and diabetic macular oedema (DME) and their clinical correlates in military personnel with type 2 diabetes (T2D), and to quantify retinal microvascular and neurosensory changes in patients without clinical DR using optical coherence tomography (OCT) and OCT angiography (OCTA).

Materials and methods. The retrospective stage included 1028 records of patients with T2D examined at the Military Hospital of the Ministry of Defence of the Republic of Uzbekistan in 2016–2025 (89.3% men; 81.5% on active service). The prospective stage included 276 participants: 30 controls without diabetes, 86 patients with T2D without clinical DR, 108 with non-proliferative DR (NPDR) and 52 with severe DR. DR was staged with the international clinical scale; DME was taken from medical records in the retrospective stage and confirmed by structural OCT in the prospective stage. Vessel density of the superficial (SCP) and deep (DCP) capillary plexuses, the foveal avascular zone (FAZ), the ganglion cell complex (GCC), the retinal nerve fibre layer and choroidal thickness were measured with a DRI OCT Triton.

Results. DR was found in 365 patients (35.5%) and DME in 82 (8.0%); DME was absent in patients without DR, and its frequency rose from 6.3% in mild NPDR to 43.2% in proliferative DR. The frequency of DR increased from 20.6% at a diabetes duration of 5 years or less to 79.2% after 15 years. In multivariable analysis, DR was associated with diabetes duration (OR 1.24 per year) and HbA1c (OR 1.48 per 1%). Compared with controls, patients without clinical DR had lower SCP (47.42 ± 1.82% vs 49.81 ± 1.78%) and DCP vessel density (52.25 ± 1.88% vs 55.41 ± 2.05%), a larger FAZ (0.309 ± 0.043 vs 0.237 ± 0.036 mm2) and a thinner GCC (88.79 ± 3.85 vs 95.79 ± 3.66 μm; all $p < 0.001$). HbA1c correlated with SCP ($r = −0.737$) and DCP density ($r = −0.731$) and with FAZ area ($r = 0.733$), and the urine albumin-to-creatinine ratio with SCP density ($r = −0.676$).

Conclusion. In military personnel with T2D, OCTA and OCT detect microvascular and neurosensory retinal changes in patients without clinical DR. In servicemen with a diabetes duration of more than 5 years or HbA1c of 7.0% or higher, the annual fundus examination should be supplemented with OCT and OCTA, and DME should be confirmed by OCT regardless of the DR stage.

Keywords: *diabetic retinopathy; type 2 diabetes; military personnel; optical coherence tomography angiography; vessel density; foveal avascular zone; ganglion cell complex*

Introduction

Diabetes mellitus affected an estimated 536.6 million adults aged 20–79 years in 2021 (10.5%), and this number is projected to reach 783.2 million by 2045 [1]. Type 2 diabetes (T2D) accounts for 96.0% of all cases [2], and its incidence among people aged 15–39 years increased from 117.22 to 183.36 per 100,000 between 1990 and 2019 [3]. Diabetic retinopathy (DR) remains a leading cause of preventable blindness in the working-age population [4, 5]. DR was present in 22.27% of people with diabetes in population-based studies [4] and in 34.6% in an earlier pooled analysis, in which diabetic macular oedema (DME) was found in 6.81% [6]. All DR end points increase with diabetes duration, HbA1c and blood pressure [6], and intensive control of glycaemia and blood pressure reduces microvascular end points [7, 8].

Military service requires good visual function, and the incidence of T2D among service members is rising: in the US active component it increased from 55.5 to 69.6 per 100,000 person-years between 2018 and 2021 [9]. Published screening data concern mainly veterans [10], and data on DR in active-duty personnel are scarce. Regional estimates depend on the setting, ranging from 23.9% of people with T2D in the national diabetes register of Kyrgyzstan [11] to 58.8% of patients with diabetes attending medical institutions in Samarkand [12].

DR is now regarded as a neurovascular complication in which neurodegeneration plays a significant role [13, 14], and in people with diabetes and no or minimal DR, progressive thinning of the nerve fibre and ganglion cell layers has been documented independently of HbA1c [15]. OCT angiography (OCTA) provides depth-resolved images of blood flow in the retina and choroid [16] and has shown enlargement of the foveal avascular zone (FAZ) and loss of capillary density in diabetic eyes before retinopathy develops [17–19]; OCTA metrics also predict DR progression and the development of DME [20]. In Uzbekistan, OCTA in patients with T2D without DR showed a 21% larger FAZ and reduced density of the deep vessels [21], but military personnel have not been

studied. The aim of this study was to determine the frequency of DR and DME and their clinical correlates in military personnel with T2D and to quantify OCT and OCTA changes in patients without clinical DR.

Materials and methods

Study design and participants

The study was carried out at the Military Hospital of the Ministry of Defence of the Republic of Uzbekistan and the DMC innovative clinic and consisted of two stages. The retrospective stage covered case histories and outpatient records for 2016–2025; records were included if they contained a diagnosis of diabetes, age, sex, service status, the year of attendance, an ophthalmological examination and the stage of DR or its absence, and all 1028 included records concerned T2D. The prospective stage (2025–2026) included 276 participants examined with a single protocol: 30 controls, 86 patients with T2D without clinical DR (no-DR group), 108 patients with non-proliferative DR (NPDR group) and 52 patients with severe DR (severe-DR group). Controls had no diabetes and no clinically significant ophthalmic disease. Marked opacity of the optic media, retinal disease of another aetiology, glaucomatous optic neuropathy, inflammatory eye disease and previous interventions affecting retinal morphometry were exclusion criteria, and images with gross motion artefacts or without a visible optic disc and macula were not analysed. Data were recorded under conditional patient codes, and the archival and prospective registers were kept separately.

Examination

All participants underwent best-corrected visual acuity testing (decimal scale), autorefractometry, Maklakov tonometry, slit-lamp biomicroscopy, ophthalmoscopy and fundus photography with a ZEISS CLARUS 500 camera (Carl Zeiss Meditec, Germany); multimodal imaging and fluorescein angiography with a SPECTRALIS HRA+OCT (Heidelberg Engineering, Germany) and automated perimetry (Humphrey Field Analyzer 3) were performed when indicated. DR was staged according to the International Clinical Diabetic Retinopathy Disease Severity Scale as no DR, mild, moderate or severe NPDR, or proliferative DR (PDR) [22]. DME was recorded separately from the DR stage, on the basis of structural OCT in the prospective stage and from medical records in the retrospective stage. Structural OCT and OCTA were performed with a DRI OCT Triton (Topcon Corporation, Japan). The macular protocol included central macular thickness (CMT), macular volume, the thickness of the ganglion cell complex (GCC), the ganglion cell–inner plexiform layer (GCL-IPL) and the inner nuclear layer (INL), and the integrity of the ellipsoid zone; the retinal nerve fibre layer (RNFL) was measured around the optic disc, and subfoveal choroidal thickness where technically possible. The OCTA protocol included vessel density in the superficial (SCP) and deep (DCP) capillary plexuses, FAZ area, perimeter and circularity index, peripapillary vessel density, the non-perfusion area and a vessel tortuosity index. The mean of both eyes was used for analysis, and vessel density was also obtained by automated image processing with the in-house RetinaRisk AI module (version 1.1.0). Diabetes duration, therapy, arterial hypertension, dyslipidaemia, nephropathy and neuropathy were recorded, and HbA1c, lipids, creatinine, estimated glomerular filtration rate (eGFR) and the urine albumin-to-creatinine ratio (UACR) obtained closest to the ophthalmological examination were used.

Statistical analysis

Quantitative variables are presented as mean ± standard deviation (SD) and categorical variables as numbers and percentages. Groups were compared with the Kruskal–Wallis test followed by pairwise Mann–Whitney tests, and categorical variables with Pearson's $\chi 2$ test or Fisher's exact test. Associations were assessed with Spearman's rank correlation and standardised coefficients (β) of linear regression. Factors associated with DR and DME were analysed with multivariable logistic regression including age, diabetes duration, HbA1c, body mass index (BMI), systolic blood pressure, arterial hypertension, dyslipidaemia, nephropathy, neuropathy, eGFR and insulin therapy, and were expressed as odds ratios (OR); model discrimination was assessed by the area under the receiver operating characteristic curve (AUC). A p value below 0.05 was considered significant.

Results

Retrospective cohort

The retrospective cohort comprised 918 men (89.3%) and 110 women (10.7%); 838 patients (81.5%) were on active military service. The mean age was 42.16 ± 6.98 years (range 23–60), the length of service 22.60 ± 7.48 years, diabetes duration 7.01 ± 4.18 years (0.4–23.0), HbA1c 7.37 ± 1.30% and eGFR 76.31 ± 14.62 mL/min/1.73 m2. DR was found in 365 patients (35.5%): mild NPDR in 111 (10.8%), moderate NPDR in 94 (9.1%), severe NPDR in 72 (7.0%) and PDR in 88 (8.6%). DME was diagnosed in 82 patients (8.0%); it was not found in patients without DR, and its frequency rose from 6.3% in mild NPDR to 18.1% in moderate NPDR, 27.8% in severe NPDR and 43.2% in PDR ($\chi 2 = 258.02$, df = 4, $p < 0.001$). Visual complaints were reported by 19.3% of patients without DR and by 92.0% of those with PDR ($p < 0.001$). The number of records increased from 88 in 2016 to 116 in 2025, and the annual frequency of DR varied between 28.9% and 44.3% without a consistent trend.

The distribution of DR stages depended on diabetes duration ($\chi 2 = 407.32$, $p < 0.001$; Figure 1). At a duration of 5 years or less, 313 of 394 patients (79.4%) had no DR, whereas after 15 years PDR was found in 31 of 48 patients (64.6%). The frequency of DR was 20.6%, 36.0%, 57.2% and 79.2% in the four duration categories, and that of DME 0.5%, 5.7%, 19.3% and 50.0% ($\chi 2 = 196.56$, $p < 0.001$). Nevertheless, 10 patients (20.8%) with a duration of more than 15 years had no DR, and 25 patients (6.3%) with a duration of 5 years or less already had moderate or more advanced DR.

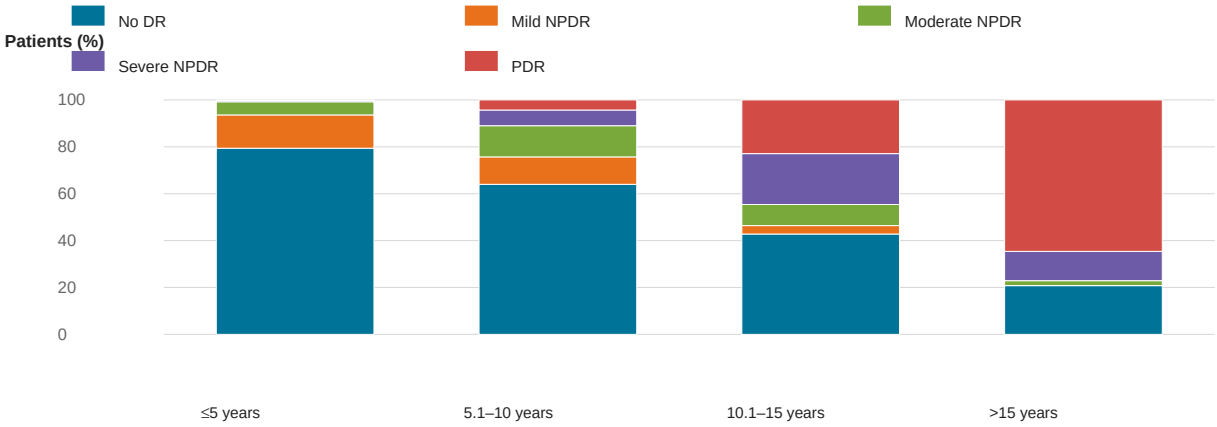


Figure 1. Distribution of diabetic retinopathy stages by diabetes duration in the retrospective cohort

n = 1028; values below 4% are not labelled. DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR.

HbA1c increased from 7.13 ± 1.18% in patients without DR to 8.96 ± 1.33% in those with PDR ($p < 0.001$; $\rho = 0.401$ with the stage, compared with $\rho = 0.452$ for diabetes duration). The proportion of patients without DR fell from 74.1% at HbA1c below 7.0% to 42.6% at 9.0% or higher, while that of PDR rose from 0.9% to 33.3%. More advanced stages were accompanied by higher systolic blood pressure, triglycerides and creatinine, lower eGFR and a higher frequency of arterial hypertension, nephropathy, neuropathy and insulin therapy, whereas BMI, dyslipidaemia, cardiovascular disease and smoking did not differ between stages (Table 1). In multivariable logistic regression, diabetes duration (OR 1.24 per year) and HbA1c (OR 1.48 per 1%) were independently associated with any DR (AUC 0.676), and the same two factors with DME (OR 1.23 and 1.61; AUC 0.831).

Table 1. Clinical characteristics by stage of diabetic retinopathy in the retrospective cohort

Parameter	No DR (n = 663)	Mild NPDR (n = 111)	Moderate NPDR (n = 94)	Severe NPDR (n = 72)	PDR (n = 88)	p
Age, years	41.71 ± 7.09	42.35 ± 7.23	42.17 ± 6.05	43.75 ± 6.59	44.03 ± 6.67	0.011
Diabetes duration, years	5.96 ± 3.49	5.29 ± 2.64	7.30 ± 2.88	10.83 ± 3.57	13.64 ± 4.15	<0.001
HbA1c, %	7.13 ± 1.18	6.80 ± 0.96	7.71 ± 1.10	8.06 ± 1.17	8.96 ± 1.33	<0.001
BMI, kg/m2	28.57 ± 3.46	28.41 ± 3.47	29.01 ± 2.63	28.74 ± 3.50	28.94 ± 3.47	0.610
Systolic BP, mmHg	125.98 ± 13.00	126.43 ± 11.84	126.19 ± 12.64	130.85 ± 11.74	129.94 ± 12.28	0.002
Triglycerides, mmol/L	1.86 ± 0.60	1.79 ± 0.66	1.92 ± 0.62	2.05 ± 0.67	2.09 ± 0.67	0.002
Creatinine, µmol/L	97.56 ± 13.55	99.10 ± 13.98	99.01 ± 13.74	103.40 ± 15.91	108.08 ± 17.59	<0.001
eGFR, mL/min/1.73 m2	77.69 ± 14.38	77.26 ± 14.63	75.27 ± 14.37	72.87 ± 13.01	68.66 ± 15.34	<0.001
Visual acuity, right eye	0.98 ± 0.14	0.90 ± 0.14	0.80 ± 0.16	0.62 ± 0.15	0.47 ± 0.15	<0.001
DME, %	0	6.3	18.1	27.8	43.2	<0.001
Visual complaints, %	19.3	27.0	39.4	55.6	92.0	<0.001
Arterial hypertension, n (%)	292 (44.0)	53 (47.7)	45 (47.9)	46 (63.9)	54 (61.4)	0.001
Dyslipidaemia, n (%)	302 (45.6)	50 (45.0)	46 (48.9)	41 (56.9)	50 (56.8)	0.136
Nephropathy, n (%)	90 (13.6)	14 (12.6)	19 (20.2)	24 (33.3)	46 (52.3)	<0.001
Neuropathy, n (%)	138 (20.8)	22 (19.8)	28 (29.8)	29 (40.3)	48 (54.5)	<0.001
Cardiovascular disease, n (%)	114 (17.2)	24 (21.6)	16 (17.0)	12 (16.7)	14 (15.9)	0.817
Insulin therapy, n (%)	304 (45.9)	43 (38.7)	50 (53.2)	42 (58.3)	67 (76.1)	<0.001
Smoking, n (%)	207 (31.2)	46 (41.4)	33 (35.1)	26 (36.1)	27 (30.7)	0.263

Note. Values are mean ± SD unless stated otherwise; p for differences between stages. DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; DME, diabetic macular oedema.

Prospective groups

The prospective groups differed in age, length of service, blood pressure, lipid levels and renal function (Table 2). Patients without clinical DR were 2.5 years older than controls (p = 0.016) and had higher HbA1c, systolic blood pressure and triglycerides and lower eGFR, whereas their UACR did not differ significantly from that of controls (p = 0.090). DME was found in 2 patients (2.3%) without clinical DR, in 40 (37.0%) with NPDR and in 45 (86.5%) with severe DR. Best-corrected visual acuity was 0.99 ± 0.02 in controls, 0.96 ± 0.05 in the no-DR group, 0.79 ± 0.08 in NPDR and 0.39 ± 0.10 in severe DR.

Table 2. Clinical characteristics of the prospective groups

Parameter	Controls (n = 30)	No DR (n = 86)	NPDR (n = 108)	Severe DR (n = 52)	p	p, controls vs no DR
Men, n (%)	28 (93.3)	73 (84.9)	97 (89.8)	49 (94.2)	—	—
Age, years	37.07 ± 5.02	39.60 ± 4.80	46.72 ± 5.37	50.71 ± 5.19	<0.001	0.016
Length of service, years	18.00 ± 5.66	20.99 ± 5.80	27.13 ± 5.95	31.50 ± 5.39	<0.001	0.009
Diabetes duration, years	—	4.61 ± 2.40	9.26 ± 2.44	14.21 ± 2.67	<0.001	—
HbA1c, %	5.39 ± 0.36	7.36 ± 0.69	8.61 ± 0.71	10.16 ± 0.68	<0.001	<0.001
Systolic BP, mmHg	118.30 ± 8.00	136.99 ± 9.63	144.93 ± 9.44	154.04 ± 12.48	<0.001	<0.001
Diastolic BP, mmHg	75.33 ± 8.31	84.23 ± 6.74	89.00 ± 5.97	91.08 ± 5.74	<0.001	<0.001
Total cholesterol, mmol/L	4.52 ± 0.48	4.98 ± 0.75	5.57 ± 0.68	5.85 ± 0.67	<0.001	0.001
Triglycerides, mmol/L	1.11 ± 0.40	1.68 ± 0.45	2.04 ± 0.42	2.34 ± 0.45	<0.001	<0.001
LDL cholesterol, mmol/L	2.64 ± 0.61	2.85 ± 0.48	3.21 ± 0.57	3.67 ± 0.43	<0.001	0.122
eGFR, mL/min/1.73 m2	85.49 ± 11.34	78.29 ± 10.01	69.01 ± 11.40	58.22 ± 10.72	<0.001	0.008
UACR, mg/g	14.19 ± 12.81	20.09 ± 16.71	44.59 ± 21.05	134.23 ± 54.41	<0.001	0.090
Arterial hypertension, n (%)	4 (13.3)	34 (39.5)	54 (50.0)	32 (61.5)	<0.001	—
Dyslipidaemia, n (%)	5 (16.7)	43 (50.0)	60 (55.6)	38 (73.1)	<0.001	—
Neuropathy, n (%)	0 (0.0)	12 (14.0)	34 (31.5)	29 (55.8)	<0.001	—
Nephropathy, n (%)	0 (0.0)	6 (7.0)	21 (19.4)	27 (51.9)	<0.001	—

Note. Values are mean ± SD unless stated otherwise; p from the Kruskal–Wallis test with post hoc Mann–Whitney tests or the χ2 test. BP, blood pressure; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; —, not applicable or not tested.

OCT angiography and structural OCT

Vessel density decreased stepwise from controls to severe DR in both plexuses and around the optic disc (Table 3, Figure 2). In patients without clinical DR, SCP density was 47.42 ± 1.82% compared with 49.81 ± 1.78% in controls and DCP density 52.25 ± 1.88% compared with 55.41 ± 2.05% (both p < 0.001). The FAZ area was 0.309 ± 0.043 mm2 compared with 0.237 ± 0.036 mm2, with a longer perimeter and a lower circularity index, and the non-perfusion area (p = 0.008) and tortuosity index (p < 0.001) were higher. Automated image processing gave almost identical vessel densities (SCP 47.39 ± 1.93% and DCP 52.28 ± 2.11% in the no-DR group). In severe DR, SCP and DCP density fell to 36.55 ± 1.62% and 38.51 ± 2.21% and the FAZ area increased to 0.665 ± 0.052 mm2.

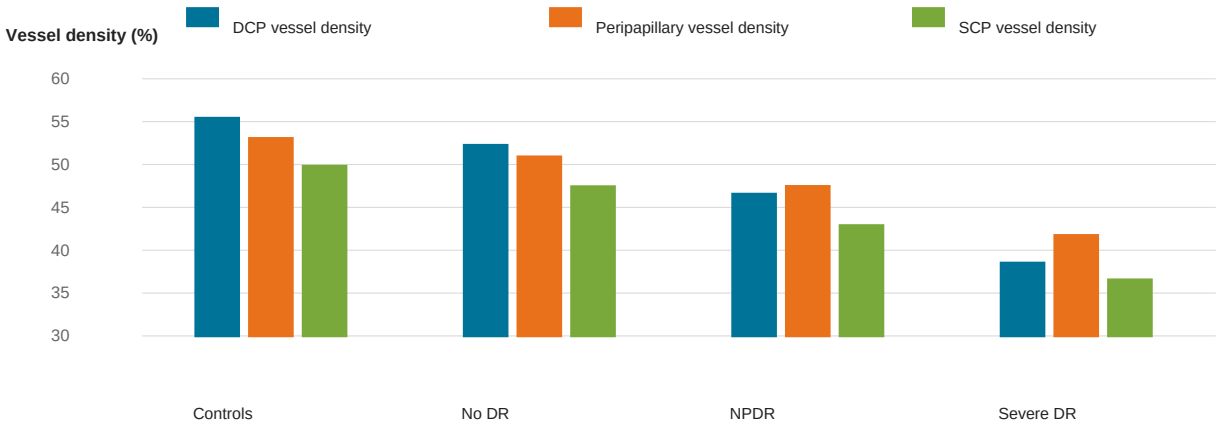


Figure 2. Retinal vessel density on OCT angiography in the prospective groups

Mean of both eyes (SD in Table 3); all differences between adjacent groups p < 0.001 (Mann–Whitney). SCP, superficial capillary plexus; DCP, deep capillary plexus; NPDR, non-proliferative diabetic retinopathy.

Table 3. OCT angiography and structural OCT parameters in the prospective groups

Parameter	Controls (n = 30)	No DR (n = 86)	NPDR (n = 108)	Severe DR (n = 52)	p (pairwise)	p (pairwise)	p (pairwise)
Parameter	Controls (n = 30)	No DR (n = 86)	NPDR (n = 108)	Severe DR (n = 52)	C vs no DR	No DR vs NPDR	NPDR vs severe
SCP VD, %	49.81 ± 1.78	47.42 ± 1.82	42.88 ± 1.53	36.55 ± 1.62	<0.001	<0.001	<0.001
DCP VD, %	55.41 ± 2.05	52.25 ± 1.88	46.55 ± 1.87	38.51 ± 2.21	<0.001	<0.001	<0.001
Peripapillary VD, %	53.05 ± 1.58	50.90 ± 1.72	47.45 ± 1.65	41.73 ± 1.20	<0.001	<0.001	<0.001
FAZ area, mm2	0.237 ± 0.036	0.309 ± 0.043	0.452 ± 0.043	0.665 ± 0.052	<0.001	<0.001	<0.001
FAZ perimeter, mm	1.893 ± 0.144	2.237 ± 0.150	2.705 ± 0.157	3.432 ± 0.159	<0.001	<0.001	<0.001
FAZ circularity index	0.875 ± 0.031	0.830 ± 0.035	0.739 ± 0.035	0.619 ± 0.042	<0.001	<0.001	<0.001
Non-perfusion area, mm2	0.057 ± 0.078	0.097 ± 0.088	0.483 ± 0.135	1.351 ± 0.143	0.008	<0.001	<0.001
Vessel tortuosity index	1.066 ± 0.042	1.146 ± 0.059	1.290 ± 0.066	1.469 ± 0.056	<0.001	<0.001	<0.001
CMT, µm	262.90 ± 15.32	273.28 ± 15.56	314.35 ± 16.03	405.26 ± 15.78	0.003	<0.001	<0.001
GCC, µm	95.79 ± 3.66	88.79 ± 3.85	80.89 ± 3.90	67.90 ± 3.16	<0.001	<0.001	<0.001
GCL-IPL, µm	88.18 ± 3.55	81.21 ± 3.98	73.30 ± 4.00	60.52 ± 3.52	<0.001	<0.001	<0.001
RNFL, µm	100.22 ± 3.62	96.73 ± 4.11	92.35 ± 4.28	83.58 ± 4.35	<0.001	<0.001	<0.001
INL, µm	34.19 ± 1.68	35.88 ± 1.65	39.37 ± 1.66	43.94 ± 1.90	<0.001	<0.001	<0.001
Choroidal thickness, µm	249.11 ± 15.57	237.03 ± 18.96	217.80 ± 20.05	188.58 ± 18.89	0.003	<0.001	<0.001

Note. Mean ± SD of both eyes; overall Kruskal–Wallis p < 0.001 for all parameters; pairwise p from Mann–Whitney tests. C, controls; VD, vessel density; other abbreviations as in the text.

Structural OCT showed thinning of the inner retinal neuronal layers in patients without clinical DR. In patients without DR, GCC thickness was 88.79 ± 3.85 µm compared with 95.79 ± 3.66 µm in controls, GCL-IPL thickness 81.21 ± 3.98 µm compared with 88.18 ± 3.55 µm, and RNFL thickness 96.73 ± 4.11 µm compared with 100.22 ± 3.62 µm (all $p < 0.001$); the INL was thicker ($p < 0.001$), CMT slightly greater ($p = 0.003$) and the choroid thinner ($p = 0.003$). Among the parameters shown in Figure 3, the largest relative differences from controls were found for FAZ area (+30.4%), FAZ perimeter (+18.2%), GCL-IPL (−7.9%), vessel tortuosity (+7.5%), GCC (−7.3%) and DCP density (−5.7%) (Figure 3). Disruption of the ellipsoid zone was found only in NPDR (20.4%) and severe DR (69.2%).

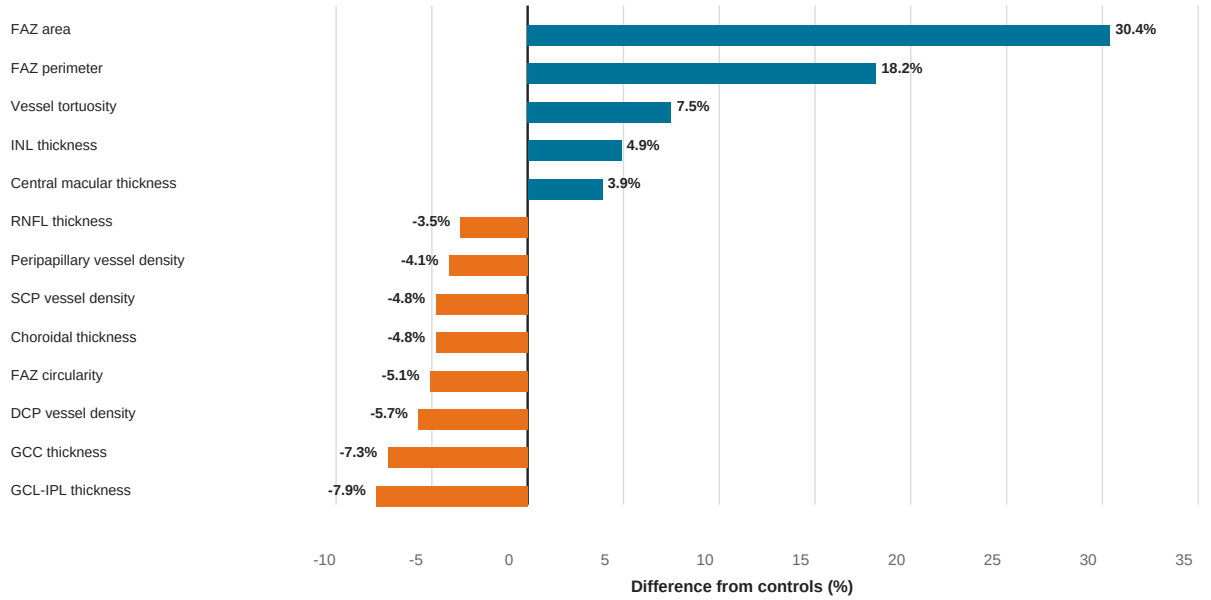


Figure 3. Subclinical retinal profile in patients with type 2 diabetes without clinical retinopathy

Relative difference = (mean in the no-DR group − mean in controls) / mean in controls × 100, calculated from the group means; all differences p ≤ 0.003 (Mann–Whitney). Abbreviations as in the text.

Correlations between systemic and retinal parameters

In the whole prospective sample, HbA1c correlated with SCP density (r = −0.737), DCP density (r = −0.731), FAZ area (r = 0.733) and CMT (r = 0.798); diabetes duration with FAZ area (r = 0.750), GCC thickness (r = −0.752) and RNFL thickness (r = −0.672); UACR with SCP density (r = −0.676); and systolic blood pressure with peripapillary vessel density (r = −0.586) (all $p < 0.001$). In multiple linear regression, HbA1c and UACR were the strongest predictors of SCP density ($R^2 = 0.778$; β = −0.406 and −0.278) and DCP density ($R^2 = 0.785$; β = −0.362 and −0.319), and diabetes duration and UACR of FAZ area ($R^2 = 0.800$; β = 0.348 and 0.317) and GCC thickness ($R^2 = 0.755$; β = −0.425 and −0.232).

Discussion

This study combined a ten-year hospital-based retrospective cohort with a prospective imaging study of military personnel with T2D. DR was found in about one third of patients and its frequency rose steeply with diabetes duration and HbA1c, while in patients without clinical DR, OCTA and OCT already showed lower capillary density, an enlarged FAZ and thinning of the inner retinal neuronal layers. Most patients were men of service age, with a mean age of 42 years, and four-fifths were on active service, so the findings concern personnel whose fitness for duty depends directly on visual function.

The frequency of DR (35.5%) is close to the 34.6% of the pooled analysis of 35 studies [6] and higher than the 22.27% estimated from population-based studies [4]. Our sample was hospital based, and clinic-based studies give higher estimates than population surveys: 31.8% in diabetes clinics and 29.6% in the general population in Iran [23] and 58.8% among patients attending medical institutions in Samarkand [12], and the pooled estimate for the Eastern Mediterranean Region was 31% [24]. The frequency of DME (8.0%) was similar to the pooled 6.81% [6]. DME was absent in patients without DR but present in 43.2% of those with PDR, which supports grading DME separately from the DR stage, as the international classification provides [22].

The relation with diabetes duration was similar to that in the Wisconsin study of patients diagnosed at 30 years or older, in which DR prevalence rose from 28.8% at a duration of less than 5 years to 77.8% at 15 years or more [25]; in our cohort it rose from 20.6% to 79.2%. The independent association with HbA1c agrees with UKPDS, in which the incidence of retinopathy was associated with baseline glycaemia and higher blood pressure [26] and each 1% reduction in HbA1c was associated with a 37% lower risk of microvascular complications [27]. Nephropathy, neuropathy and reduced eGFR accompanied the more severe stages; DR is consistently associated with other complications of diabetes [28], and patients with UACR above 30 mg/g had a 58.5% higher risk of vision-threatening DR in a meta-analysis of cohort studies [29].

In patients without clinical DR, vessel density was lower in both plexuses, with a larger relative deficit in the DCP (−5.7%) than in the SCP (−4.8%). Meta-analyses confirm lower SCP and DCP density in eyes without DR, with weighted mean differences of −1.34 and −2.00 percentage points [30], and reduced perfusion of both macular plexuses and around the optic disc, particularly in T2D [19]. In several studies the DCP was affected first: in one, only DCP density was reduced in T2D without DR and it correlated with diabetes duration (R = −0.52) [31], and in an Uzbek cohort the decrease in the deep plexus also occurred earlier [32]. Other authors observed earlier changes in the SCP [33], so the sequence may depend on the device and the analysed region.

The FAZ was 30% larger than in controls, with a longer perimeter and lower circularity. FAZ enlargement in diabetic eyes without retinopathy was reported by Takase et al. (0.37 vs 0.25 mm2) [17], de Carlo et al. [34] and Dimitrova et al. [18] and confirmed by meta-analysis [19], but the FAZ did not differ from controls in some studies of T2D [35, 36] or in another meta-analysis [30]. Because the FAZ varies widely in healthy eyes (0.07–0.434 mm2 in one control group [34]) and its area discriminated diabetic eyes poorly in another study [37], it is more informative together with vessel density and at follow-up. Lower FAZ circularity was associated with GCL-IPL thinning in diabetic eyes [38], and capillary non-perfusion and peripapillary vessel loss have been described before retinopathy [34, 39, 40]; the increased vessel tortuosity in our no-DR group, previously linked mainly to NPDR [41], needs confirmation. With advancing DR, all OCTA parameters in our patients changed stepwise, in line with studies in which almost all OCTA parameters correlated linearly with DR severity [42] and the superficial FAZ was larger in DR than in normal eyes (0.518 vs 0.339 mm2) [43]; superficial vessel density distinguished eyes with DR from healthy eyes best of the four OCTA metrics tested, with an area under the curve of 0.893 [37]. In severe DR, the non-perfusion area in our patients reached 1.351 mm2 and the FAZ circularity index fell to 0.619, reflecting advanced macular ischaemia.

GCC and GCL-IPL were 7–8% thinner in patients without DR, which agrees with evidence that retinal neurodegeneration may precede microvascular changes [15]; ganglion cell layer thinning has been shown in patients with minimal DR with type 1 and type 2 diabetes [44, 45], although macular GCC was comparable to controls in one study of T2D without DR [46]. The INL was thicker, as reported in eyes with NPDR and interpreted as Müller cell activation [47]; the INL is also the layer most thickened in subclinical macular oedema [48], whereas another study found the INL thinner in eyes without DR [49]. The thinner choroid agrees with a meta-analysis showing a 14.34 μm thinner subfoveal choroid in diabetic eyes without retinopathy [50]; however, the choroid became progressively thinner with DR severity in our patients, whereas another meta-analysis found it thicker in DR than in eyes without DR [51].

Retinal microvascular parameters correlated closely with HbA1c, diabetes duration and UACR. Lower vessel density has been associated with higher HbA1c [52, 53], although other studies found no such correlation [35, 37]. The association with UACR agrees with the Kailuan Eye Study, in which lower vessel and perfusion density in diabetes without DR was associated with higher UACR [54], and with reduced SCP density in microalbuminuric patients [55], suggesting that retinal capillary loss reflects systemic microangiopathy. Hypertension is also associated with lower retinal vessel density [56], and the higher blood pressure in our diabetic groups may have contributed to the differences.

OCTA metrics have prognostic value: a larger FAZ and lower DCP density predicted DR progression, and lower SCP density predicted DME [20]. The American Academy of Ophthalmology recommends at least yearly examination in T2D [57], whereas the American Diabetes Association allows examinations every 2 years after one or more normal annual examinations [58]. For servicemen, whose duties depend on visual function, our findings support adding OCT and OCTA to the annual examination when diabetes has lasted more than 5 years or HbA1c is 7.0% or higher, and confirming DME by OCT, which also detects subclinical macular oedema [48]; in a military eye service, a single non-mydriatic photograph showed only moderate agreement with ophthalmoscopy for DR ($\kappa = 0.44$) [59]. Automated analysis of fundus images has reached high sensitivity and specificity in large studies [60, 61] and could support screening in military medical units if its results are verified by an ophthalmologist. As a working criterion for patients without visible DR, the combination of DCP density below 52%, FAZ area above 0.30 mm2 and GCC thickness below 90 μm, values close to the means of our no-DR group, may be used to shorten the follow-up interval to 6 months even when visual acuity is preserved; these thresholds require validation in longitudinal studies.

The strengths of the study are the large retrospective cohort covering ten years, the measurement of structural and angiographic parameters with a single protocol and device, and the verification of vessel density by automated image processing. The study also has limitations. The retrospective data came from a single military hospital, so the frequency of DR may be higher than among all service members with diabetes. The prospective part was cross-sectional, the groups differed in age, blood pressure and lipid levels, which were not adjusted for in the group comparisons, and the control group was small and younger. OCTA values depend on the device and segmentation, and the prognostic value of the subclinical changes requires longitudinal follow-up.

Conclusion

In military personnel with T2D treated at a military hospital, DR was found in 35.5% and DME in 8.0%, and both increased with diabetes duration and HbA1c. In patients without clinical DR, OCTA showed lower SCP and DCP vessel density and an enlarged FAZ, and OCT showed thinning of the GCC and GCL-IPL, indicating early microvascular and neurosensory damage; across the prospective sample, these parameters correlated with HbA1c, diabetes duration and albuminuria. OCT and OCTA should supplement the annual fundus examination of servicemen with T2D of more than 5 years' duration or HbA1c of 7.0% or higher, and DME should be confirmed by OCT regardless of the DR stage.

References

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119. doi:10.1016/j.diabres.2021.109119

2. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023;402(10397):203-34. doi:10.1016/S0140-6736(23)01301-6

3. Xie J, Wang M, Long Z, Ning H, Li J, Cao Y, et al. Global burden of type 2 diabetes in adolescents and young adults, 1990-2019: systematic analysis of the Global Burden of Disease Study 2019. BMJ. 2022;379:e072385. doi:10.1136/bmj-2022-072385

4. Teo ZL, Tham YC, Yu M, Chee ML, Rim TH, Cheung N, et al. Global Prevalence of Diabetic Retinopathy and Projection of Burden through 2045: Systematic Review and Meta-analysis. Ophthalmology. 2021;128(11):1580-91. doi:10.1016/j.ophtha.2021.04.027

5. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet. 2010;376(9735):124-36. doi:10.1016/S0140-6736(09)62124-3

6. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35(3):556-64. doi:10.2337/dc11-1909

7. UK Prospective Diabetes Study (UKPDS) Group. 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. 1998;352(9131):837-53. doi:10.1016/S0140-6736(98)07019-6

8. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998;317(7160):703-13. doi:10.1136/bmj.317.7160.703

9. Stiegmann RA, Payne CB, Kiel MA, Stahlman SL. Increased Prevalence of Overweight and Obesity and Incidence of Prediabetes and Type 2 Diabetes During the COVID-19 Pandemic, Active Component Service Members, U.S. Armed Forces, 2018 to 2021. MSMR. 2023;30(1):11-8.

10. Davis M, Snider MJE, Hunt KJ, Medunjanin D, Neelon B, Maa AY. Geographic variation in diabetic retinopathy screening within the Veterans Health Administration. Prim Care Diabetes. 2023;17(5):429-35. doi:10.1016/j.pcd.2023.06.004

11. Sultanalieva RB, Abylova NK, Zhunusova BZ. [Role of the state register of diabetes mellitus in assessing the epidemiological situation in Kyrgyzstan and Bishkek]. Probl Endokrinol (Mosk). 2025;71(2):55-65. Russian. doi:10.14341/probl13502

12. Allayarov AT, Rizaev ZhA, Yusupov AA. [Frequency of diabetic retinopathy in the population of Samarkand]. Advanced Ophthalmology. 2024;8(2):123-5. Russian. doi:10.57231/j.ao.2024.8.2.024

13. Simó R, Stitt AW, Gardner TW. Neurodegeneration in diabetic retinopathy: does it really matter? Diabetologia. 2018;61(9):1902-12. doi:10.1007/s00125-018-4692-1

14. Wong TY, Cheung CM, Larsen M, Sharma S, Simó R. Diabetic retinopathy. Nat Rev Dis Primers. 2016;2:16012. doi:10.1038/nrdp.2016.12

15. Sohn EH, van Dijk HW, Jiao C, Kok PH, Jeong W, Demirkaya N, et al. Retinal neurodegeneration may precede microvascular changes characteristic of diabetic retinopathy in diabetes mellitus. Proc Natl Acad Sci U S A. 2016;113(19):E2655-64. doi:10.1073/pnas.1522014113

16. Spaide RF, Fujimoto JG, Waheed NK, Sadda SR, Staurenghi G. Optical coherence tomography angiography. Prog Retin Eye Res. 2018;64:1-55. doi:10.1016/j.preteyeres.2017.11.003

17. Takase N, Nozaki M, Kato A, Ozeki H, Yoshida M, Ogura Y. Enlargement of foveal avascular zone in diabetic eyes evaluated by en face optical coherence tomography angiography. Retina. 2015;35(11):2377-83. doi:10.1097/IAE.0000000000000849

18. Dimitrova G, Chihara E, Takahashi H, Amano H, Okazaki K. Quantitative Retinal Optical Coherence Tomography Angiography in Patients With Diabetes Without Diabetic Retinopathy. Invest Ophthalmol Vis Sci. 2017;58(1):190-6. doi:10.1167/iovs.16-20531

19. Zhang B, Chou Y, Zhao X, Yang J, Chen Y. Early Detection of Microvascular Impairments With Optical Coherence Tomography Angiography in Diabetic Patients Without Clinical Retinopathy: A Meta-analysis. Am J Ophthalmol. 2021;222:226-37. doi:10.1016/j.ajo.2020.09.032

20. Sun Z, Tang F, Wong R, Lok J, Szeto SKH, Chan JCK, et al. OCT Angiography Metrics Predict Progression of Diabetic Retinopathy and Development of Diabetic Macular Edema: A Prospective Study. Ophthalmology. 2019;126(12):1675-84. doi:10.1016/j.ophtha.2019.06.016

21. Yangieva NR, Tuychibaeva DM, Urmanova FM. [Study of OCTA angiography in type 2 diabetes without signs of diabetic retinopathy]. Advanced Ophthalmology. 2023;4(4):65-9. Russian. doi:10.57231/j.ao.2023.4.4.011

22. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003;110(9):1677-82. doi:10.1016/S0161-6420(03)00475-5

23. Sadat Mahmoudi Nezhad G, Razeghinejad R, Janghorbani M, Mohamadian A, Hassan Jalalpour M, Bazdar S, et al. Prevalence, Incidence and Ecological Determinants of Diabetic Retinopathy in Iran: Systematic Review and Meta-analysis. J Ophthalmic Vis Res. 2019;14(3):321-35. doi:10.18502/jovr.v14i3.4790

24. Heiran A, Azarchehry SP, Dehghankhalili S, Afarid M, Shaabani S, Mirahmadizadeh A. Prevalence of diabetic retinopathy in the Eastern Mediterranean Region: a systematic review and meta-analysis. J Int Med Res. 2022;50(10):3000605221117134. doi:10.1177/03000605221117134

25. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol. 1984;102(4):527-32. doi:10.1001/archopht.1984.01040030405011

26. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, et al. UKPDS 50: risk factors for incidence and progression of retinopathy in Type II diabetes over 6 years from diagnosis. Diabetologia. 2001;44(2):156-63. doi:10.1007/s001250051594

27. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-12. doi:10.1136/bmj.321.7258.405

28. Pearce I, Simó R, Lövestam-Adrian M, Wong DT, Evans M. Association between diabetic eye disease and other complications of diabetes: Implications for care. A systematic review. Diabetes Obes Metab. 2019;21(3):467-78. doi:10.1111/dom.13550

29. Liang Y, Zhang X, Mei W, Li Y, Du Z, Wang Y, et al. Predicting vision-threatening diabetic retinopathy in patients with type 2 diabetes mellitus: Systematic review, meta-analysis, and prospective validation study. J Glob Health. 2024;14:04192. doi:10.7189/jogh.14.04192

30. Yang F, Zou W, Li Z, Du Y, Gao W, Zhang J, et al. Optical coherence tomography angiography for detection of microvascular changes in early diabetes: A systematic review and meta-analysis. Diabetes Metab Res Rev. 2024;40(4):e3812. doi:10.1002/dmrr.3812

31. Altinisik M, Kahraman NS, Kurt E, Mayali H, Kayikcioglu O. Quantitative analysis of early retinal vascular changes in type 2 diabetic patients without clinical retinopathy by optical coherence tomography angiography. Int Ophthalmol. 2022;42(2):367-75. doi:10.1007/s10792-022-02230-8

32. Bakhritdinova FA, Urmanova FM, Tuychibaeva DM. [Diagnostic role of angiography optical coherent tomography in diabetic retinopathy]. Advanced Ophthalmology. 2023;2(2):29-34. Russian. doi:10.57231/j.ao.2023.2.2.005

33. Santos T, Santos AR, Almeida AC, Rocha AC, Reste-Ferreira D, Marques IP, et al. Retinal Capillary Nonperfusion in Preclinical Diabetic Retinopathy. Ophthalmic Res. 2023;66(1):1327-34. doi:10.1159/000534553

34. de Carlo TE, Chin AT, Bonini Filho MA, Adhi M, Branchini L, Salz DA, et al. Detection of microvascular changes in eyes of patients with diabetes but not clinical diabetic retinopathy using optical coherence tomography angiography. Retina. 2015;35(11):2364-70. doi:10.1097/IAE.0000000000000882

35. Cao D, Yang D, Huang Z, Zeng Y, Wang J, Hu Y, et al. Optical coherence tomography angiography discerns preclinical diabetic retinopathy in eyes of patients with type 2 diabetes without clinical diabetic retinopathy. Acta Diabetol. 2018;55(5):469-77. doi:10.1007/s00592-018-1115-1

36. Oliverio GW, Ceravolo I, Bhatti A, Trombetta CJ. Foveal avascular zone analysis by optical coherence tomography angiography in patients with type 1 and 2 diabetes and without clinical signs of diabetic retinopathy. Int Ophthalmol. 2021;41(2):649-58. doi:10.1007/s10792-020-01621-z

37. Durbin MK, An L, Shemonski ND, Soares M, Santos T, Lopes M, et al. Quantification of Retinal Microvascular Density in Optical Coherence Tomographic Angiography Images in Diabetic Retinopathy. JAMA Ophthalmol. 2017;135(4):370-6. doi:10.1001/jamaophthalmol.2017.0080

38. Kim K, Kim ES, Yu SY. Optical coherence tomography angiography analysis of foveal microvascular changes and inner retinal layer thinning in patients with diabetes. Br J Ophthalmol. 2018;102(9):1226-31. doi:10.1136/bjophthalmol-2017-311149

39. Vujosevic S, Muraca A, Gatti V, Masoero L, Brambilla M, Cannillo B, et al. Peripapillary Microvascular and Neural Changes in Diabetes Mellitus: An OCT-Angiography Study. Invest Ophthalmol Vis Sci. 2018;59(12):5074-81. doi:10.1167/iovs.18-24891

40. Jin H, Wang K, Ren C, He S, Gao Y, Liang X, et al. Early peripapillary neurovascular injury and its relevant systemic factors in type 2 diabetic patients without retinopathy: An OCTA based study. Photodiagnosis Photodyn Ther. 2025;54:104716. doi:10.1016/j.pdpdt.2025.104716

41. Lee H, Lee M, Chung H, Kim HC. Quantification of retinal vessel tortuosity in diabetic retinopathy using optical coherence tomography angiography. Retina. 2018;38(5):976-85. doi:10.1097/IAE.0000000000001618

42. Nesper PL, Roberts PK, Onishi AC, Chai H, Liu L, Jampol LM, et al. Quantifying Microvascular Abnormalities With Increasing Severity of Diabetic Retinopathy Using Optical Coherence Tomography Angiography. Invest Ophthalmol Vis Sci. 2017;58(6):BIO307-BIO315. doi:10.1167/iovs.17-21787

43. Al-Sheikh M, Akil H, Pfau M, Sadda SR. Swept-Source OCT Angiography Imaging of the Foveal Avascular Zone and Macular Capillary Network Density in Diabetic Retinopathy. Invest Ophthalmol Vis Sci. 2016;57(8):3907-13. doi:10.1167/iovs.16-19570

44. van Dijk HW, Verbraak FD, Kok PH, Garvin MK, Sonka M, Lee K, et al. Decreased retinal ganglion cell layer thickness in patients with type 1 diabetes. Invest Ophthalmol Vis Sci. 2010;51(7):3660-5. doi:10.1167/iovs.09-5041

45. van Dijk HW, Verbraak FD, Kok PH, Stehouwer M, Garvin MK, Sonka M, et al. Early neurodegeneration in the retina of type 2 diabetic patients. Invest Ophthalmol Vis Sci. 2012;53(6):2715-9. doi:10.1167/iovs.11-8997

46. Zeng Y, Cao D, Yu H, Yang D, Zhuang X, Hu Y, et al. Early retinal neurovascular impairment in patients with diabetes without clinically detectable retinopathy. Br J Ophthalmol. 2019;103(12):1747-52. doi:10.1136/bjophthalmol-2018-313582

47. Vujosevic S, Midena E. Retinal layers changes in human preclinical and early clinical diabetic retinopathy support early retinal neuronal and Müller cells alterations. J Diabetes Res. 2013;2013:905058. doi:10.1155/2013/905058

48. Bandello F, Tejerina AN, Vujosevic S, Varano M, Egan C, Sivaprasad S, et al. Retinal layer location of increased retinal thickness in eyes with subclinical and clinical macular edema in diabetes type 2. Ophthalmic Res. 2015;54(3):112-7. doi:10.1159/000438792

49. Shah J, Tan B, Wong D, Abdul Gani NFB, Hu Q, Liu X, et al. Evaluation of thickness of individual macular retinal layers in diabetic eyes from optical coherence tomography. Sci Rep. 2024;14(1):17909. doi:10.1038/s41598-024-68552-y

50. Endo H, Kase S, Saito M, Yokoi M, Takahashi M, Ishida S, et al. Choroidal Thickness in Diabetic Patients Without Diabetic Retinopathy: A Meta-analysis. Am J Ophthalmol. 2020;218:68-77. doi:10.1016/j.ajo.2020.05.036

51. Jiang J, Liu J, Yang J, Jiang B. Optical coherence tomography evaluation of choroidal structure changes in diabetic retinopathy patients: A systematic review and meta-analysis. Front Med (Lausanne). 2022;9:986209. doi:10.3389/fmed.2022.986209

52. Xie N, Tan Y, Liu S, Xie Y, Shuai S, Wang W, et al. Macular vessel density in diabetes and diabetic retinopathy with swept-source optical coherence tomography angiography. Graefes Arch Clin Exp Ophthalmol. 2020;258(12):2671-9. doi:10.1007/s00417-020-04832-3

53. Li H, Yu X, Zheng B, Ding S, Mu Z, Guo L. Early neurovascular changes in the retina in preclinical diabetic retinopathy and its relation with blood glucose. BMC Ophthalmol. 2021;21(1):220. doi:10.1186/s12886-021-01975-7

54. Wang Q, Liu L, Jonas JB, Gao B, Wu SL, Chen SH, et al. Albuminuria and retinal vessel density in diabetes without diabetic retinopathy: the Kailuan Eye Study. Acta Ophthalmol. 2021;99(5):e669-e678. doi:10.1111/aos.14670

55. Cankurtaran V, Inanc M, Tekin K, Turgut F. Retinal Microcirculation in Predicting Diabetic Nephropathy in Type 2 Diabetic Patients without Retinopathy. Ophthalmologica. 2020;243(4):271-9. doi:10.1159/000504943

56. Tan W, Yao X, Le TT, Tan ACS, Cheung CY, Chin CWL, et al. The Application of Optical Coherence Tomography Angiography in Systemic Hypertension: A Meta-Analysis. Front Med (Lausanne). 2021;8:778330. doi:10.3389/fmed.2021.778330

57. Flaxel CJ, Adelman RA, Bailey ST, Fawzi A, Lim JI, Vemulakonda GA, et al. Diabetic Retinopathy Preferred Practice Pattern®. Ophthalmology. 2020;127(1):P66-P145. doi:10.1016/j.ophtha.2019.09.025

58. Solomon SD, Chew E, Duh EJ, Sobrin L, Sun JK, VanderBeek BL, et al. Diabetic Retinopathy: A Position Statement by the American Diabetes Association. Diabetes Care. 2017;40(3):412-8. doi:10.2337/dc16-2641

59. Chun DW, Bauer RM, Ward TP, Dick JS, Bower KS. Evaluation of digital fundus images as a diagnostic method for surveillance of diabetic retinopathy. Mil Med. 2007;172(4):405-10. doi:10.7205/milmed.172.4.405

60. Gulshan V, Peng L, Coram M, Stumpe MC, Wu D, Narayanaswamy A, et al. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. JAMA. 2016;316(22):2402-10. doi:10.1001/jama.2016.17216

61. Abràmoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. NPJ Digit Med. 2018;1:39. doi:10.1038/s41746-018-0040-6