



Evaluation of radial peripapillary capillary density in patients with newly diagnosed iron deficiency anemia

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Abstract

Purpose To investigate the effects of iron deficiency anemia (IDA) on radial peripapillary capillary vessel density (RPCvd) and retinal nerve fiber layer (RNFL) thickness.

Methods Forty patients with IDA, and 46 healthy participants, were enrolled in this study. Optical coherence tomography angiography was used to determine RNFL thickness and RPCvd measurements. In addition, hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and ferritin laboratory values were evaluated.

Results Analysis of retinal regions (whole images, peripapillary, superior-hemi, inferior-hemi, inferior-nasal, inferior-temporal, temporal-inferior, temporal-superior, superior-nasal) showed that RPCvd values were significantly lower in patients with IDA compared to the control group values ($p < 0.05$ for all).

However, there were no significant differences in RNFL thickness values between the IDA patient group and the control group ($p > 0.05$ for all). In addition, there were significant positive correlations between RPCvd values and hematological values for Hb, HCT, MCV, MCH, MCHC, and ferritin.

Conclusion It is important to identify changes in retinal vascularity to prevent possible ocular problems in patients with IDA. Specifically, the significant positive correlations between RPCvd values and hematological values suggest that anemia treatment is important for optic nerve perfusion.

Keywords Iron deficiency anemia · Optical coherence tomography angiography · Retinal nerve fiber layer · Radial peripapillary capillary

Introduction

Anemia is a disease that leads to a lowering of the blood's oxygen-carrying capacity, and it is a significant and widespread public health problem [1, 2]. Iron deficiency anemia (IDA) is the most common cause of anemia in children, women of childbearing age, and in pregnancy [3, 4]. In IDA, defined by a low concentration of hemoglobin (Hb) in the blood, hypoxia is inevitable since the vascular system cannot carry adequate oxygen throughout the body. As a consequence of hypoxia, detrimental effects have been

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reported in various systems of the body, including the eye [5].

Both neural and vasculature changes in the retinas of anemic patients have been determined in recent studies. Several studies have shown the effects of anemia on ocular structures, especially the posterior segment of the eye [6–10]. A higher risk for developing diabetic retinopathy was detected in anemic diabetic patients compared to non-anemic diabetic patients [11], and proliferative retinopathy has been reported in both sickle cell anemia and thalassemia [11, 12]. Choroidal thickness was determined to be thinner in IDA patients compared to healthy subjects [7, 13], and the thickness of the peripapillary retinal nerve fiber layer (RNFL) was reduced in anemic patients compared to healthy subjects [8, 9]. Anemia is considered to be a significant factor for the progression, or development, of optic neuropathies via its vascular and neural effects.

Optical coherence tomography angiography (OCT-A) is a method that allows for the evaluation of the radial peripapillary capillary (RPC) network [14]. OCT-A is a noninvasive imaging technique that allows for the quantitative evaluation of microvascular structures using a split spectrum amplitude-decorrelation angiography analytical algorithm.

The aim of the present study was to evaluate the thickness of the RNFL and the RPC vessel density (RPCvd) in patients with IDA using the OCT-A system, and to compare these results with those of age- and sex-matched healthy control subjects.

Methods

This prospective cross-sectional study was performed in the Department of Ophthalmology at the Ulucanlar Eye Training and Research Hospital, and at the Internal Medicine Clinic of Ankara Training and Research Hospital, between February 2019 and December 2019. The study protocol was approved by the Ethics Committee of the Ankara Training and Research Hospital, and the study was conducted in accordance with the ethical principles of the Helsinki Declaration. Informed written consent was obtained from all the participants.

Patients with IDA, and age- and sex-matched control subjects, who referred to our ophthalmology clinic from the Internal Medicine Clinic of Ankara

Training and Research Hospital were enrolled as study group and control group, respectively. The diagnosis of IDA was determined by laboratory findings: serum Hb level < 13 g/dl in men and < 12 g/dl in women; mean corpuscular volume (MCV) of < 80 fL; mean corpuscular hemoglobin (MCH) of < 23 pg/erythrocyte; mean corpuscular hemoglobin concentration (MCHC) of < 32 g/dl; serum ferritin < 30 ng/ml; and serum transferrin saturation of < 15% [15]. Subjects without the abnormal laboratory findings described above were included in the study as controls.

All control subjects who had any systemic or ocular disease were excluded from the study. Additionally, patients who had any ocular disease, and any systemic disease other than IDA, were also excluded from the study. Subjects with a best corrected visual acuity (BCVA) equal to or greater than 20/20 according to the Snellen chart, and no history of any ocular problem other than refractive errors equal to or less than 1.00 diopter spherical equivalent, were included in the study. Participants with a history of smoking, drug, and alcohol consumption, and any ocular surgery were excluded from the study.

All patients underwent a detailed ophthalmological examination including assessment of BCVA according to the Snellen chart, anterior segment examination with slit-lamp biomicroscopy, a dilated fundus examination, and measurement of intraocular pressure using non-contact tonometry. After pupil dilation, subjects were seated in front of an OCT-A scanner (XR Avanti AngioVue; Version 2017.1.0.151; Optovue, Fremont, California, USA), asked to fixate on its internal target, and then examined. All subjects underwent optic disk area measurement using the optic nerve head (ONH) scan protocol. AngioVue disk mode was used to obtain optic disk OCT-A images using 4.5×4.5 mm fields. The device used two ONH-centered concentric circles with diameters of 2 mm (inner) and 4 mm (outer) to automatically calculate RPCvd (%) and RNFL thickness (μm) between these rings (Fig. 1). The OCT-A device provided these measurement values in eight equal 45 degree sectors (superior-nasal (SN), superior-temporal (ST), temporal-superior (TS), temporal-inferior (TI), nasal-superior (NS), nasal-inferior (NI), inferior-nasal (IN) and inferior-temporal (IT) and two equal hemispheres (superior-hemi and inferior-hemi). In addition to these RPCvd measurements, vessel densities of inside the disk, and of the whole image were

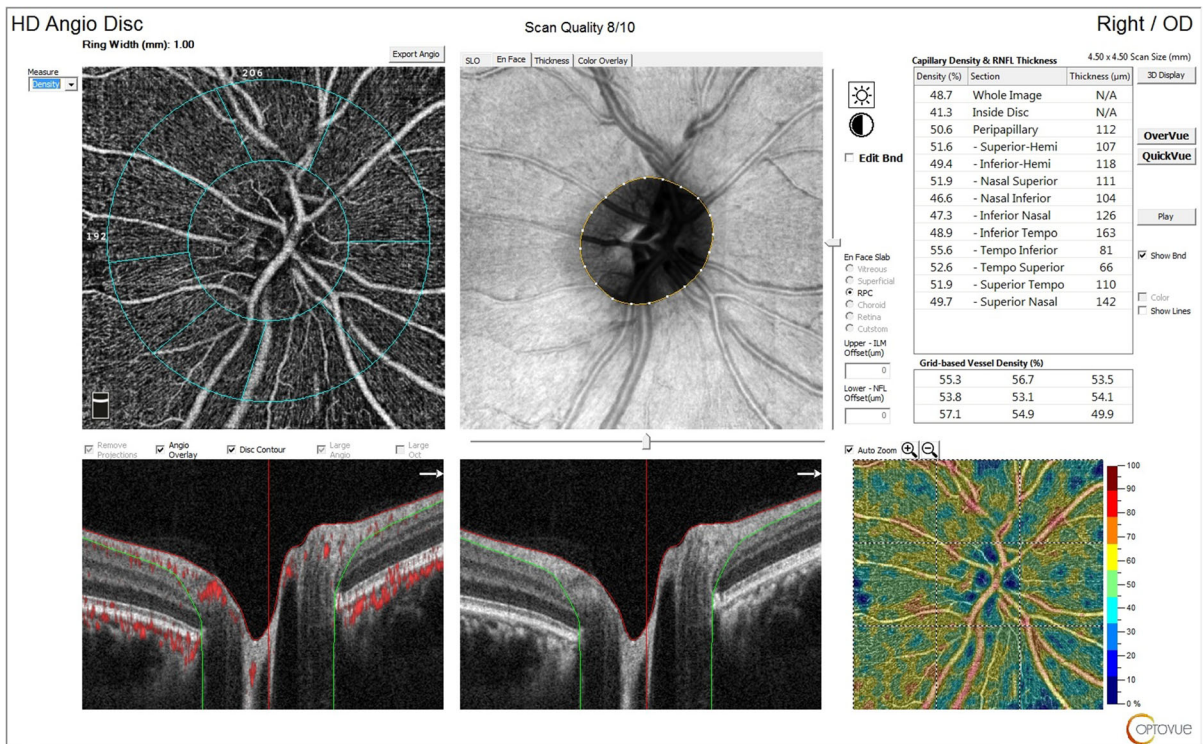


Fig. 1 OCT-A device attaches two optic nerve head (ONH) centered concentric circles with a diameter of 2 mm (inner) and 4 mm (outer) and calculates radial peripapillary capillary vessel

density (RPCvd) (%) and RNFL thickness (μm) between these concentric circles automatically. The scan size was received 4.5×4.5 mm in this study

also calculated, and segmentation was automatically located between the inner limiting membrane and the RNFL to calculate RPCvd values. Patient retinal images with poor characteristics, such as a low signal-strength index ($\text{SSI} < 8$), blink artifacts, motion or doubling artifacts, and segmentation errors were not included in the study. Only the right eye of each subject was analyzed.

Statistical analyses

For statistical analyses, SPSS 24.0 software for Windows (SPSS Inc., Chicago, IL) was used to analyze outcomes. Descriptive statistics are presented as means \pm standard deviations, with values for minimum and maximum data. Categorical variables between groups were analyzed using the χ^2 test. The distribution pattern of the variables was tested by visual (histogram and probability graphs) and analytical (Kolmogorov–Smirnov/Shapiro–Wilk test) tools. Independent-sample t tests were used for normally distributed data, and the Mann–Whitney U test was

used for non-normally distributed data. Correlations between parameters were tested either by the Pearson correlation test for normally distributed data, or the Spearman correlation test for non-normally distributed data. A p value less than 0.05 was considered statistically significant.

Results

Forty patients (35 female, 5 male) with a diagnosis of IDA, and 46 age- and sex-matched healthy subjects (37 female, 9 male) were enrolled in this case–control study. The mean age was 42.2 ± 9.4 years (range 29–74) in the patient group and 45.8 ± 10.7 years (range 23–68) in the control group. The age and sex characteristics of both group were similar ($p = 0.107$ and $p = 0.141$ respectively).

The hematological features of the IDA and control groups are shown in Table 1. There were significant differences in all blood serum findings between the

Table 1 Hematological features of IDA and control groups

	IDA group (n = 40) Mean ± SD (min–max)	Control group (n = 46) Mean ± SD (min–max)	p value ^a
Erythrocyte (million/ μ L)	4.53 ± 0.54 (3.6–6.6)	4.83 ± 0.35 (4.2–5.8)	0.003
Hb (g/dL)	9.28 ± 1.45 (6.5–10.4)	13.90 ± 1.15 (12.5–17.5)	< 0.001
HCT (%)	31.99 ± 3.40 (24.0–38.0)	42.13 ± 3.68 (35.9–53.0)	< 0.001
MCV (fL)	70.49 ± 10.66 (31.0–82.8)	85.68 ± 3.41 (78.0–95.0)	< 0.001
MCH (pg/erythrocyte)	20.73 ± 3.61 (15.0–27.0)	27.92 ± 1.55 (24.2–31.0)	< 0.001
MCHC (g/dL)	28.84 ± 2.00 (25.0–31.7)	32.38 ± 1.20 (30.0–35.0)	< 0.001
RDW (%)	18.17 ± 2.65 (13.4–25.9)	13.87 ± 2.02 (12.0–22.0)	< 0.001
Ferritin (μ g/L)	6.23 ± 6.02 (2.2–15.7)	25.89 ± 17.23 (7.6–125.0)	< 0.001
Iron (μ g/dL)	30.80 ± 16.03 (13.0–65.0)	69.20 ± 25.33 (37.01–00.0)	0.003
UIBC (μ g/dL)	404.9 ± 69.7 (271–511)	317.6 ± 69.8 (226–420)	0.04
TIBC (μ g/dL)	435.7 ± 57.6 (336–526)	381.4 ± 42.4 (326–430)	0.087
TSAT (%)	7.54 ± 4.98 (2.9–14.4)	18.64 ± 8.50 (8.0–31.0)	0.007
Transferrin (mg/dL)	3.04 ± 0.40 (2.3–3.6)	2.75 ± 0.42 (2.28–3.2)	0.254

IDA Iron-deficiency anemia, Hb Hemoglobin, HCT Hematocrit, MCV Mean cell volume, MCH Mean corpuscular hemoglobin, MCHC Mean corpuscular hemoglobin concentration, RDW Red blood cell distribution width, UIBC Unsaturated iron-binding capacity, TIBC Total iron-binding capacity, TSAT Transferrin saturation, SD Standard deviation

^aStudent *t* test

IDA group and the control group, except for total iron-binding capacity and transferrin levels.

The RPCvd values for the IDA and control groups are shown in Table 2. RPCvd values for whole images, peripapillary, superior-hemi, inferior-hemi, IN, IT, TI, TS, and SN areas were significantly lower in patients with IDA compared to the control group ($p < 0.05$ for all). There were no significant differences in RNFL

thickness values between the patient group and the control group ($p > 0.05$ for all) (Table 3).

Tables 4 and 5 show the correlations between blood serum findings, RNFL thickness, and RPCvd values. There were a limited number of significant correlations between RNFL thickness and hematological parameters, including red cell distribution width (RDW), MCV, and MCH. However, there were

Table 2 Radial peripapillary capillary density of IDA and control groups

	RPCvd (%)	IDA group (n = 40) Mean ± SD (min–max)	Control group (n = 46) Mean ± SD (min–max)	p value ^a
Whole image		49.5 ± 2.8 (41.9–54.7)	50.9 ± 2.0 (44.1–53.8)	0.011
Inside disk		50.2 ± 3.9 (41.5–57.5)	50.7 ± 4.8 (41.3–62.0)	0.586
Peripapillary		51.1 ± 3.5 (43.9–57.9)	53.3 ± 2.3 (48.0–56.6)	0.001
Superior hemi		51.3 ± 3.9 (41.5–57.2)	53.3 ± 2.4 (48.3–57.4)	0.006
Inferior hemi		50.8 ± 3.4 (42.0–59.3)	53.4 ± 2.5 (47.5–57.8)	< 0.001
Nasal-superior		49.3 ± 4.9 (37.7–59.7)	50.3 ± 3.8 (42.3–56.7)	0.266
Nasal-inferior		47.5 ± 4.5 (37.8–57.0)	49.1 ± 4.5 (38.8–57.0)	0.093
Inferior-nasal		49.7 ± 5.0 (39.7–62.8)	54.0 ± 3.4 (45.9–61.3)	< 0.001
Inferior-temporal		56.3 ± 4.3 (43.2–65.4)	58.7 ± 3.2 (53.4–67.1)	0.005
Temporal-inferior		51.0 ± 3.9 (40.2–60.2)	53.0 ± 3.9 (43.8–59.7)	0.021
Temporal-superior		54.0 ± 4.0 (46.6–62.3)	55.9 ± 2.8 (49.5–59.9)	0.016
Superior-temporal		54.1 ± 5.3 (44.4–62.7)	56.4 ± 3.3 (47.8–62.3)	0.114 ^b
Superior-nasal		48.5 ± 4.7 (37.9–58.1)	51.7 ± 3.4 (45.9–61.8)	0.001

RPCvd Radial peripapillary capillary vessel density, IDA Iron-deficiency anemia, SD Standard deviation

^aStudent *t* test, ^bMann–Whitney *U* test

Table 3 Retinal nerve fiber layer thickness of IDA and control groups

	RNFL (μ)	IDA group (n = 40) Mean \pm SD (min–max)	Control group (n = 46) Mean \pm SD (min–max)	<i>p</i> value ^a
	Peripapillary	114.5 \pm 19.3 (94–186)	113.6 \pm 10.3 (94–144)	0.805
	Superior hemi	117.1 \pm 23.6 (93–208)	112.6 \pm 10.4 (91–143)	0.253
	Inferior hemi	111.8 \pm 16.0 (91–166)	114.6 \pm 12.0 (93–148)	0.357
	Nasal-superior	122.2 \pm 33.7 (88–253)	111.7 \pm 17.4 (74–160)	0.069
	Nasal-inferior	99.0 \pm 21.9 (62–177)	93.3 \pm 15.6 (68–132)	0.170
	Inferior-nasal	141.0 \pm 24.9 (99–209)	148.1 \pm 22.3 (94–205)	0.177
	Inferior-temporal	139.2 \pm 27.3 (100–226)	147.6 \pm 23.0 (99–224)	0.130
	Temporal-inferior	65.3 \pm 11.4 (45–93)	69.1 \pm 11.9 (46–110)	0.145
	Temporal-superior	70.8 \pm 15.1 (19–126)	73.5 \pm 10.9 (50–106)	0.351
	Superior-temporal	129.7 \pm 23.7 (96–220)	129.7 \pm 21.1 (85–169)	0.998
	Superior-nasal	142.0 \pm 44.1 (11–282)	139.0 \pm 17.6 (107–181)	0.678

RNFL Retinal nerve fiber layer, IDA Iron-deficiency anemia, SD Standard deviation

^aStudent *t* test

numerous significant positive correlations between RPCvd values and hematological parameters, including Hb, HCT, MCV, MCH, MCHC, and ferritin. Only one significant negative correlation was determined between RDW and RPCvd values.

Discussion

IDA is one of the most common nutritional deficiencies in the world, and it is characterized by blood's insufficient capacity to carry oxygen in the body [16]. The pathological effects of anemia can be seen in various body systems, including the effects of hypoxia on the eye [5]. In the present study, we investigated the effects of IDA on RNFL thickness and RPCvd using OCT-A assessment.

Recent studies have shown a variety of ocular disorders in patients with IDA, such as central retinal vein occlusion, papilledema, retinal hemorrhage, and ischemic retinopathy [17, 18]. In addition, both Simsek et al. [7] and Yumusak et al. [13] reported choroid thinning in IDA patients compared to healthy subjects. The neural RNFL is another tissue element reported to become thinner in IDA patients compared to the normal population [8, 9], and iron deficiency can affect retinal dopaminergic neurotransmitter dysfunction [19]. Similarly, Monga et al. [20] reported longer latencies in visually evoked potentials in anemic pediatric patients. Moreover, investigations of β -thalassemia by Heyderian et al. [21] concluded that pathological ocular changes such as retinopathy, reduced visual acuity, and color vision deficiency

could be consequences of anemia. All of these perspectives suggest that tissue hypoxia and pathological ocular outcomes are inevitable due to anemia [22].

The RNFL and RPC network have a prominent neurovascular relationship around the ONH. The nourishment of the RNFL is provided by the RPC network [23, 24], and this neurovascular relationship is important for normal ganglion cell function [25, 26]. Glaucoma is a common ocular disease characterized by retinal ganglion cell degeneration and decreased RNFL thickness [27]. The vascular hypothesis of glaucoma is that retinal ganglion cell axons undergo oxygen insufficiency as a result of compromised local blood flow, ultimately leading to their degeneration [28]. Chen et al. [29] determined that ONH blood flow was lower in patients with open-angle glaucoma than in control subjects, and that there were correlations between structural changes in the optic nerve and RNFL blood flow. Similarly, Hwang et al. [30] found a significant correlation between decreased retinal blood flow and disease severity in glaucomatous eyes. Even without glaucoma, reduced RNFL thickness has been found in hypoxia-associated diseases such as obstructive sleep apnea syndrome [31]. Taken together, these studies support the idea of reduced RNFL thickness under hypoxic conditions.

Various animal models have also been used to investigate the effects of hypoxia on the retina. Kurihara et al. [32] used animal models in which hypoxia could be genetically induced in the retinal pigmented epithelium and showed that hypoxia-induced metabolic stress resulted in photoreceptor

Table 4 Correlations between hematological features and radial peripapillary capillary density values

<i>r^s</i>	Erythrocyte (million/ μ L)	Hb (g/dL)	HCT (%)	MCV (fL)	MCH (pg/eryth)	MCHC (g/dL)	RDW (%)	Ferritin (μ g/L)	Iron (μ g/dL)	UIBC (μ g/dL)	TIBC (μ g/dL)	TSAT (%)	Transferrin (mg/dL)
Radial peripapillary capillary density													
	– .270*	0.267*	0.172	0.414**	0.456**	0.401**	– .447**	0.202	0.053	0.042	0.064	0.006	0.073
	– 0.211	0.078	0.045	0.178	0.198	0.155	– .245*	0.090	– 0.078	0.097	0.071	– 0.108	0.138
	– 0.140	0.346**	0.257*	0.414**	0.482**	0.433**	– .444**	0.268*	0.040	0.023	0.031	– 0.005	0.009
	– 0.143	0.328**	0.249*	0.400**	0.467**	0.425**	– .413**	0.251*	0.116	– 0.044	– 0.010	0.056	– 0.080
	– 0.114	0.337**	0.245*	0.390**	0.452**	0.401**	– .437**	0.265*	0.009	0.066	0.064	– 0.028	0.080
	– .278*	0.113	0.019	0.238*	0.285**	0.284**	– .276*	0.205	– 0.135	– 0.014	– 0.072	– 0.158	– 0.138
	– 0.159	0.151	0.055	0.220*	0.270*	0.247*	– .322**	0.213	0.132	– 0.070	– 0.061	0.095	– 0.024
	– 0.054	0.387**	0.301**	0.400**	0.474**	0.463**	– .430**	0.356**	0.156	– 0.176	– 0.201	0.136	– 0.168
	– 0.053	0.245*	0.205	0.273*	0.303**	0.228*	– .282**	0.146	– 0.153	0.110	0.053	– 0.130	0.018
	– 0.070	0.228*	0.197	0.283**	0.301**	0.242*	– .242*	0.021	– 0.288	0.554*	0.622*	– 0.364	0.614*
	– 0.004	0.353**	0.312**	0.352**	0.408**	0.343**	– .347**	0.142	0.202	0.127	0.273	0.147	0.301
	– 0.121	0.164	0.137	0.210	0.205	0.204	– .220*	0.293**	0.034	– 0.058	– 0.062	0.081	– 0.124
	0.003	0.419**	0.383**	0.466**	0.510**	0.450**	– .419**	0.258*	0.306	– 0.173	– 0.100	0.227	– 0.219

Hb Hemoglobin, *HCT* Hematocrit, *MCV* Mean cell volume, *MCH* Mean corpuscular hemoglobin, *MCHC* Mean corpuscular hemoglobin concentration, *RDW* Red blood cell distribution width, *UIBC* Unsaturated iron-binding capacity, *TIBC* Total iron-binding capacity, *TSAT* Transferrin saturation

^aPearson correlation coefficient, ^bSpearman correlation coefficient

Bold values indicate statistically significant correlations ($p < 0.05$, ** $p < 0.01$)

Table 5 Correlations between hematological features and retinal nerve fiber layer thickness values

r^a	Erythrocyte (million/ μ L)	Hb (g/dL)	HCT (%)	MCV (fL)	MCH (pg/eryth)	MCHC (g/dL)	RDW (%)	Ferritin (μ g/L)	Iron (μ g/dL)	UIBC (μ g/dL)	TIBC (μ g/dL)	TSAT (%)	Transferrin (mg/dL)
Radial peripapillary capillary density													
	-0.228*	-0.059	-0.100	0.045	0.044	0.033	-0.159	-0.072	-0.121	-0.020	-0.071	-0.109	-0.069
Superior-hemi	-0.220*	-0.124	-0.153	-0.033	-0.035	-0.044	-0.100	-0.161	-0.162	-0.015	-0.086	-0.141	-0.097
Inferior-hemi	-0.213	0.030	-0.023	0.136	0.135	0.125	-0.214*	0.054	-0.063	-0.011	-0.028	-0.065	-0.003
Nasal-superior	-0.250*	-0.184	-0.194	-0.052	-0.072	-0.093	-0.078	-0.131	-0.046	-0.130	-0.190	-0.048	-0.193
Nasal-inferior	-0.143	-0.165	-0.196	-0.116	-0.106	-0.085	-0.034	0.018	0.120	-0.211	-0.214	0.123	-0.197
Inferior-nasal	-0.174	0.045	0.001	0.137	0.127	0.101	-0.174	0.102	0.183	-0.286	-0.318	0.197	-0.283
Inferior-temporal	-0.148	0.132	0.089	0.212	0.217*	0.208	-0.252*	-0.006	-0.374	0.357	0.343	-0.386	0.373
Temporal-inferior	-0.106	0.146	0.131	0.236*	0.224*	0.206	-0.153	0.014	-0.369	0.443	0.457	-0.419	0.430
Temporal-superior	-0.041	0.105	0.049	0.090	0.121	0.129	-0.137	-0.048	-0.003	-0.032	-0.026	0.028	0.033
Superior-temporal	-0.098	-0.002	-0.045	-0.023	0.052	0.061	-0.110	-0.163	-0.045	0.014	0.002	-0.013	0.045
Superior-nasal	-0.109	-0.055	-0.074	-0.006	-0.025	-0.017	-0.057	-0.066	-0.331	0.117	0.010	-0.299	-0.052

Hb Hemoglobin, *HCT* Hematocrit, *MCV* Mean cell volume, *MCH* Mean corpuscular hemoglobin, *MCHC* Mean corpuscular hemoglobin concentration, *RDW* Red blood cell distribution width, *UIBC* Unsaturated iron-binding capacity, *TIBC* Total iron-binding capacity, *TSAT* Transferrin saturation

^aPearson correlation coefficient

Bold values indicate statistically significant correlations ($p < 0.05$, $**p < 0.01$)

degeneration. In addition, an increased contribution of calpain enzymes to monkey retinal ganglion cell death was found in the RNFL of hypoxic retinal cultures [33], and reduced blood flow to the ONH has been shown to exacerbate ganglion cell axonal injury in rats [28].

In the present study, RPCvd values in various regions (whole retinal imaging, peripapillary, superior-hemi, inferior-hemi, IN, IT, TI, TS, and SN) were found to be significantly lower in patients with IDA compared to control group values, but assessment of RNFL thickness was similar in both groups. Additionally, we found a variety of significant correlations between RPCvd and hematological parameters (Hb, HCT, MCV, MCH, MCHC, RDW, and ferritin), but also a small number of correlations between RNFL thickness values and hematological parameters (MCV, MCH, and RDW). Based on these results, we speculate that IDA leads to a decrease in ONH vascular capillaries, resulting in RPCvd that is more affected than RNFL thickness, and that the extent of these vascular structural changes may vary depending on anemia severity.

Similar to the present study in adults, Korkmaz et al. [34] investigated the effects of IDA on peripapillary vessel density in children using OCT-A assessment, and their results also showed a reduced RPCvd in the pediatric IDA group compared to controls. However, while RNFL thickness was not investigated, they also reported a positive correlation between MCV and ferritin values and RPCvd values, similar to the present study.

To the best of our knowledge, this is the first published study to investigate the effect of IDA on RPCvd in adult patients using OCT-A. A strength of the study was the prospective nature of patient recruitment. However, the study also had several limitations. The first was that the study population included a wide age range, although there were no statistically significant differences between groups. In addition, we think that an investigation of the ganglion cell layer complex and the use of visually evoked potentials may have further contributed to our results. Finally, we were unable to fully evaluate patients due to low follow-up compliance after anemia treatments.

In conclusion, it is crucial to identify any changes in retinal vascularity to prevent possible ocular problems in IDA patients. The present study showed that RPCvd was lower in IDA patients compared to control

subjects, and there were significant correlations between anemia severity and RPCvd. Wide-ranging and post-treatment studies should be conducted in the future to determine relationships between the IDA severity and retinal vascular structure, and also in IDA patients with optic neuropathies such as glaucoma.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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