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ORIGINAL ARTICLE

The quantification of retinal vein and artery trajectories using second-order polynomial equation in eyes with diabetic retinopathy

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Abstract

Purpose: The objective of this study was to quantify retinal artery (RA) and vein trajectory alterations using a quadratic polynomial model, which may reveal associations with diabetic retinopathy (DR) severity and glycated hemoglobin (HbA1c) levels.

Methods: This study aimed to quantify the RA and vein trajectory in DR using the quadratic polynomial equation. The ideal curves of the right (OD) and left (OS) eyes for the RA and retinal vein (RV) trajectories were determined. The transformed coordinates were applied to a quadratic polynomial (ax2/100 + bx + c) equation. The coefficient 'a' denotes the curvature of the vascular path; larger values indicate a steeper, narrower curve, whereas smaller values indicate a broader, flatter curve, which may be associated with retinal retraction or tractional changes.

Results: The analysis involved 320 eyes of 167 patients, 74 males and 93 females, with a mean age of 58.1 years (34–76 years). Background, preproliferative, and proliferative DR (BDR, PPDR, PDR) were assessed. HbA1C levels were higher in PDR than in BDR ($p<0.05$). Retinal artery trajectory (RAT) in OD "a" values were higher in control than BDR, PPDR, and PDR. ($p<0.05$) RV trajectory in OD values was lower in PDR ($p=0.031$). Positive correlations existed between HbA1C levels and "a" value of RAT in OS and the mean value of RAT for both eyes in PDR ($r=0.737$, $p=0.002$; $r=0.669$, $p=0.006$).

Conclusion: These alterations in RAT, particularly in PDR, may reflect underlying tractional forces and could potentially serve as non-invasive markers of disease severity. However, further research is needed to fully understand their clinical implications and relationship with the HbA1C level.

Keywords: Diabetes mellitus; diabetic retinopathy; proliferative diabetic retinopathy; retinal artery trajectory; retinal vein trajectory.

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Diabetic retinopathy (DR) is one of the leading causes of vision loss worldwide, especially in the West. It causes findings and complications such as retinal hemorrhage, neovascularization, and vitreous hemorrhage, primarily due to chronic hyperglycemia and imbalances in the amount of vascular endothelial growth factor (VEGF) in the retina, and the occurrence of complications makes the management of the disease very difficult.[1] The multifactorial pathogenesis of DR encompasses chronic hyperglycemia, dysregulation of VEGF, and inflammatory processes, which collectively instigate retinal microangiopathy and subsequent complications. The vessel wall is affected, leading to occlusion of capillaries, retinal ischemia, and leakage, which can be quickly confirmed with angiography. The non-proliferative phase of DR sees the onset of intraluminal, intramural, and extravascular changes characterized by microangiopathy. When the disease progresses to the proliferative stage, new vessels can be observed both in the vitreoretinal interface and in the vitreous, as well as fibrovascular tissue proliferation on the retinal surface and optic disc. Proliferative alterations are observed in roughly 50% of individuals with type 1 diabetes, 5–10% of those with non-insulin-dependent type 2 diabetes, and 30% of patients with insulin-dependent type 2 diabetes.[2] Tractional forces in DR affect the retinal vasculature as well as all the layers of the retina and may alter the vascular trajectory. Therefore, even if noticeable tractional changes are not observed in the early stages of the disease, it is difficult to know what subclinical changes have occurred.

Prior studies demonstrated that the tangential traction force at the macula results in an elongation of the retinal artery trajectory (RAT).[3] To the best of our knowledge, it is unknown to what extent the possible tractional forces occurring at different stages of the disease may affect the retinal vasculature. This study aimed to investigate the effects of DR on the retinal vasculature trajectory with a different methodology.

Materials and Methods

Participants

Data from patients with DR identified at Haseki Training and Research Hospital between January 2022 and December 2022 were analyzed in this retrospective, cross-sectional, case–control study. One thousand four hundred sixty patients were scanned in the retina unit. A total of 1250 patients were screened in the retina unit. From these, patients diagnosed with DR and with fundus images of sufficient quality were considered eligible. To avoid inter-eye staging variability, only patients whose both eyes were at the same DR stage (background diabetic retinopathy [BDR], pre-proliferative diabetic retinopathy [PPDR], or proliferative diabetic retinopathy [PDR]) were included. Among the eligible pool, a stratified random selection process was employed. Using an online randomization tool (https://www.randomizer.org), patient IDs were stratified by DR stage, selected, and analyzed fundus images of 250 eyes from 125 treatment-naive DR patients. Seventy fundus photographs of 42 participants without intraocular pathology were determined as the control group by the same method. All randomizations were carried out by an independent researcher blinded to the study hypothesis. Participants with photos of both eyes showing the same stage of DR were included in the study. Eyes with ophthalmic conditions that could affect fundus findings including epiretinal membrane (ERM), posterior vitreous detachment, vitreomacular traction (VMT), prior laser photocoagulation, or any intraocular surgery other than uncomplicated cataract surgery were excluded. DR was divided into three categories: BDR, PPDR, PDR.[4]

Measurement of RAT and RV Trajectory (RVT)

The RAT computation was assessed using the second-order polynomial equation formulated by Yoshihara et al.[3] Color fundus images were captured using a fundus camera system. (Zeiss, Oberkochen, Germany). To place the retinal arteries vertically, the color fundus pictures were rotated 90° clockwise for the right eye and 90° counterclockwise for the left. The paths of the RA and retinal vein (RV) were manually delineated along the vascular arcades on the fundus photographs using at least 20 points. The RA originated from the optic disc at the location indicated by the first dot. The "invert Y coordinate" feature of the ImageJ software (accessible at http://imagej.nih.gov/ij/; ImageJ version 1.47; National Institutes of Health, Bethesda, MD, USA) automatically produced the "x" and "y" coordinates. The ImageJ curve-fitting application was utilized to fit the transformed coordinate data to the 2nd° polynomial equation, $ax^2/100 + bx + c$. The curve-fitting tool of ImageJ generated the specified constants a, b, and c. The coefficient of the quadratic polynomial "a" denotes the curvature of the arterial curve. A larger 'a' denotes a narrower/steeper trajectory (arms closer to the fovea); a smaller 'a' denotes a broader/flatter trajectory. Plotting was carried out as follows in the eyes where the retinal

arteries branch: If a branch artery was smaller than the main artery, the RAT was computed using the principal artery. The plotting was not conducted post-branching if the branch artery was comparable in size to the main artery. In each example, a minimum of 20 points was used to plot the data. The same formula used to calculate the RAT curve fits was applied to the RVT (Figs. 1 and 2). To avoid measurement bias, the same person (AA) estimated all the RAT and RVT readings. All trajectory measurements were performed by a single experienced ophthalmologist using a standardized protocol. The examiner has previously conducted similar measurements with high consistency.[5] These calculations were completed by both the right (OD) and left (OS) eyes. The average value of both eyes was also calculated. This study was approved by the Institutional Review Board and Ethics Committee of Haseki Training and Research Hospital (no. 179-2022). The methods complied with the principles of the Helsinki Declaration. Informed consent was waived due to the retrospective nature of the study.

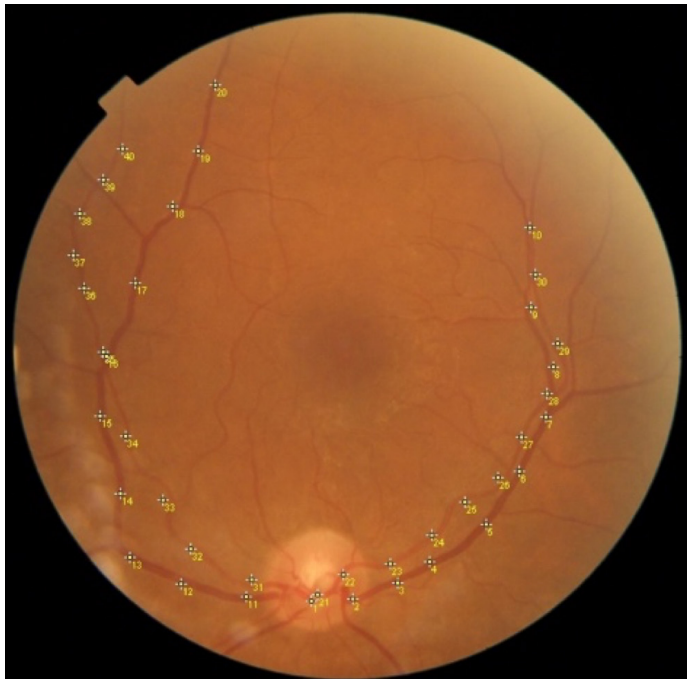

Fig. 1. Figuring out the retinal vessel trajectory's coordinates. The color fundus photos have their fovea-disk axis vertically rotated. The colored fundus picture showed the locations of the retinal vessels. The pixel coordinate values were automatically calculated using ImageJ software and then transformed into a new dataset with the optic disk center as the origin. The retinal artery trajectory is represented by coordinates 21–40, which exhibit a narrower curve compared to the vein trajectories (coordinates 1–20).

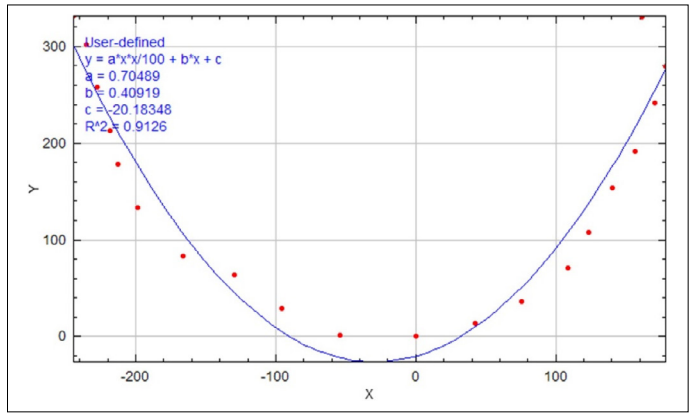

Fig. 2. The converted coordinates were fit to a user-defined 2nd° polynomial equation, $ax^2/100+bx+c$, using ImageJ's curve fitting program.

Statistical Analyses

Descriptive statistics employed mean, standard deviation, median, minimum, maximum value, frequency, and percentage. The Kolmogorov–Smirnov test was employed to assess the distribution of variables. Analysis of variance (Tukey test) and Kruskal–Wallis tests were employed to compare quantitative data. Spearman correlation analysis was employed for the correlation assessment. A post hoc power analysis was performed based on the observed group differences in the primary outcome measures. The computed effect size (Cohen's f) was 1.77, and the resulting statistical power was 1.00 at α=0.05, confirming the adequacy of the sample size. Statistical Packages for the Social Sciences (SPSS) 28.0 (SPSS Inc., IBM, Armonk, NY, USA) was used for statistical analyses.

Results

Analysis was made of 320 eyes of 167 patients, comprising 74 males and 93 females, with a mean age of 58.1 years (34–76 years). BDR was determined in 42 eyes, PPDR in 42 eyes, and PDR in 41 eyes. A sex and age-similar control group of 42 eyes was formed. Age and gender distribution did not differ significantly among the Control, BDR, PPDR, and PDR groups ($p>0.05$). While the glycated hemoglobin (HbA1C) level was markedly higher in the PDR group compared to the BDR group ($p<0.05$), no significant difference was observed between the PPDR and PDR groups ($p>0.05$) (Table 1). There was a substantial difference in the "a" value of RAT OD values among the groups ($p=0.013$). In subgroup analysis, "a" value of RAT OD was significantly higher in the control group compared to the BDR, PPDR, and PDR groups ($p<0.05$). No significant differences were found among the groups regarding the "a" value of RAT OS and RAT mean. RVT OD values

Table 1. Descriptive statistics of demographic features, HbA1C levels, and retinal trajectory parameters in the study population

	Min-Max	Median	Mean±SD/n(%)
Age	34.0–76.0	58.0	58.1±7.3
Gender			
Male			74±44.3
Female			93±55.7
HbA1C	6.00–13.90	8.85	9.24±1.84
RAT			
OD	0.13–1.20	0.51	0.54±0.22
OS	0.11–1.51	0.53	0.54±0.20
Mean	0.17–1.32	0.52	0.54±0.19
RVT			
OD	0.15–1.46	0.66	0.66±0.23
OS	0.12–1.39	0.62	0.65±0.24
Mean	0.15–1.10	0.66	0.65±0.18
Group			
Control			42 (25.1%)
BDR			42 (25.1%)
PPDR			42 (25.1%)
PDR			41 (24.6%)

OD: Right eye; OS: Left eye; RAT: Retinal artery trajectory; RVT: Retinal vein trajectory; SD: Standard deviation; HbA1C: Glycated hemoglobin.

were significantly lower in the PDR group than in other groups (p=0.031) (Table 2 and Fig. 3). Significant positive correlations were observed between HbA1C levels and "a" value of RAT OS and RAT mean in the PDR group (r=0.737, p=0.002; r=0.669, p=0.006), whereas no correlations were observed among the other parameters (Table 3). In both RAT and RVT measurements, no significant correlation was observed between the right and left eyes across all groups (Table 4).

Discussion

DR remains a formidable global health challenge, representing a leading cause of vision impairment and blindness, particularly in developed nations.[6,7] The analysis unveiled significant variations in the "a" value of RAT in the right eye among groups (p=0.013), demonstrating a lower "a" value in all DR groups compared to the control group (p<0.05). In addition, reduced RVT values, characterized by more comprehensive vessel calibration in the right eye, were also noted in PDR cases (p=0.031). In all three groups of DR, dilation in the RAT was observed, yet statistically significant differences were only evident in the right eye. It is anticipated that any traction in these structures will alter the course of the retinal vasculature. When the "a" number is modest, the vessels' parabola forms tend to be steeper and broader, signifying a greater distance between the vessels and the fovea. The non-proliferative phase of DR is characterized by intraretinal hemorrhage, microaneurysm, increased venous caliber, intraretinal microaneurysm anomaly, neuronal infarcts represented by lipid exudate, cotton wool spots, capillary non-perfusion, and retinal vascularization. Histopathological changes are observed as a reduction in endothelial cell pericytes and thickening of the basilar membrane.[8] Depending on the rheological properties of the blood, a decrease in fibrinolysis, an increase in blood viscosity, a reduction in serum albumin concentration, and an increase in fibrinogen, platelet, and alpha-2 globulin concentrations can also be observed.[9] Changes in VEGF concentration due to ischemia cause PDR, characterized by forming new vessels and tractional membranes.[10] One of the hallmarks of DR is the transition from the non-proliferative phase to the proliferative phase, marked by the formation of new blood vessels on the retina and optic disc. This neovascularization, driven in part by the upregulation of angiogenic factors such as VEGF, can lead to severe visual impairment if left untreated. In addition to neovascularization, the proliferative phase of DR is associated with fibrovascular proliferation, which can result in tractional forces on the retina and vitreous, further exacerbating retinal damage and compromising visual function. Tractional forces in DR have been implicated in a range of retinal abnormalities, including alterations in retinal vascular trajectory. Previous studies have demonstrated that tangential traction at the macula can broaden the RAT, suggesting that tractional forces may significantly shape retinal vascular morphology.[5] However, the extent to which tractional forces contribute to retinal vascular changes at different stages of DR remains poorly understood. Even in the non-proliferative phase, subtle changes that may lead to subclinical tractional forces can expand the trajectory despite the absence of apparent tractional forces. However, the statistical difference observed solely in the right eye could be attributed to the relatively small size of the study population and the asymmetric localization of findings in eyes from the same individual, despite being in the same stage. This asymmetric pattern of vascular trajectory alteration, particularly the statistically significant difference in the right eye, suggests lateralized vascular involvement in DR. To our knowledge, this is the first study to demonstrate such laterality in vascular curvature changes among DR stages, suggesting that disease severity may exert differential effects even in clinically symmetrical eyes. Several factors may underlie this asymmetry, including physiological differences in

Table 2. Comparison of age, gender, HbA1C, and retinal trajectory parameters across diabetic retinopathy stages and control group

	[1]Control group	[2]BDR group	[3]PPDR group	[4]PDR group	p
Age					
Mean±SD	59.5±6.5	58.9±7.5	57.8±8.3	55.6±6.7	0.081[K]
Median	60.0	59.0	58.5	55.0	
Gender					
Male, n-%	20 (47.6%)	24 (57.1%)	17 (40.5%)	13 (31.7%)	
Female, n-%	22 (52.4%)	18 (42.9%)	25 (59.5%)	28 (68.3%)	
HbA1C					
Mean±Sd	N/A	8.4±1.5	9.3±2.2	10.4±1.4	0.003[K]
Median	N/A	8.0[4]	8.8	10.7	
RAT					
OD					
Mean±SD	0.63±0.23	0.50±0.19	0.53±0.22	0.51±0.23	0.013[K]
Median	0.62	0.45[1]	0.48[1]	0.45[1]	
OS					
Mean±SD	0.58±0.24	0.53±0.19	0.52±0.16	0.54±0.22	0.746[K]
Median	0.56	0.51	0.53	0.50	
Mean					
Mean±SD	0.60±0.21	0.52±0.17	0.53±0.17	0.51±0.19	0.067[K]
Median	0.63	0.48	0.52	0.47	
RVT					
OD					
Mean±SD	0.70±0.22	0.64±0.24	0.70±0.26	0.58±0.18	0.031[K]
Median	0.69	0.63	0.71	0.5913	
OS					
Mean±SD	0.67±0.24	0.64±0.24	0.64±0.19	0.65±0.27	0.970[A]
Median	0.62	0.62	0.63	0.58	
Mean					
Mean±SD	0.69±0.16	0.64±0.19	0.68±0.18	0.60±0.19	0.170[A]
Median	0.68	0.64	0.67	0.59	

A ANOVA / K Kruskal-Wallis (Mann-Whitney U test) / X^2 Chi-square test; Difference with 1Control group P<0.05, Difference with 3Stage-II group P<0.05; Difference with 4Stage-III group P<0.05; OD: Right eye; OS: Left eye; RAT: Retinal artery trajectory; RVT: Retinal vein trajectory; SD: Standard deviation; BDR: Background Diabetic Retinopathy; PPDR: Preproliferative Diabetic Retinopathy; PDR: Proliferative Diabetic Retinopathy.

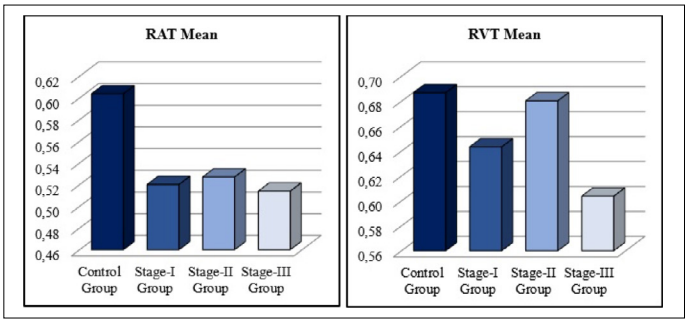

Fig. 3. The mean of the "a" value of retinal artery trajectory and retinal vein trajectory among the groups.

ocular vascular structure between eyes, such as variations in arterial branching, mechanical tension patterns, or perfusion gradients. Furthermore, despite including only bilaterally symmetrical DR stages, subclinical anatomical or functional asymmetry may persist. The limited sample size may also have contributed to the differential statistical significance observed. Notably, although the difference in the mean value of RAT was not statistically significant, it approached significance (p=0.067). In this case, tractional forces in PDR may affect RVs in the last stage, as in retinal arteries.

In light of this understanding, Yoshihara et al.[3] conducted an exploration with 155 macular hole (MH) patients. They discovered that the "a" value of RAT in MH eyes was smaller than in the other eyes, which a broader and flatter RAT explained. A separate study by Ma et al.[11] found that compared to healthy control individuals, the RAT was much broader in the contralateral eyes of patients with unilateral ERM (p<0.001). Yucel Gencoglu et al.[5] similarly reported

Table 3. Spearman correlation between HbA1C and retinal artery/vein trajectory parameters within each DR stage

	RAT OD	RAT OS	RAT mean	RVT OD	RVT OS	RAT mean
HbA1C						
BDR Group						
r	0.243	−0.003	0.160	0.127	−0.016	0.039
P	0.265	0.990	0.477	0.562	0.942	0.865
PPDR Group						
r	−0.238	−0.398	−0.405	0.058	−0.204	−0.077
P	0.413	0.159	0.170	0.837	0.505	0.802
PDR Group						
r	0.307	0.737	0.669	0.156	−0.257	−0.209
P	0.247	0.002	0.006	0.563	0.374	0.473
Total						
r	0.094	0.033	0.068	0.072	−0.214	−0.138
P	0.503	0.820	0.640	0.607	0.140	0.345

RAT: Retinal artery trajectory; RVT: Retinal vein trajectory; OD: Right eye; OS: Left eye; r: Spearman correlation coefficient; P: P-value; BDR: Background Diabetic Retinopathy; PPDR: Preproliferative Diabetic Retinopathy; PDR: Proliferative Diabetic Retinopathy.

Table 4. Correlation between retinal artery and vein trajectory parameters in control and DR groups (OD and OS separately)

	RAT and RVT correlation	
	OD	OS
Control group		
r	0.026	0.186
P	0.874	0.245
BDR Group		
r	−0.039	−0.024
P	0.806	0.886
PPDR Group		
r	0.077	0.285
P	0.654	0.079
PDR Group		
r	0.274	−0.029
P	0.091	0.860
Total		
r	0.156	0.101
P	0.052	0.207

RAT: Retinal artery trajectory; RVT: Retinal vein trajectory; OD: Right eye; OS: Left eye; r: Spearman correlation coefficient; P: P-value; BDR: Background Diabetic Retinopathy; PPDR: Preproliferative Diabetic Retinopathy; PDR: Proliferative Diabetic Retinopathy.

a higher "a" value for RVT in VMT. The authors explained this by suggesting a centrifugal force in the macula may elevate the "a" value of RVT. It is unknown what subclinical alterations in PDR or non-PDR may arise from this scenario, and it is also unknown what sort of modifications the retinal vascular system may undergo despite the lack of studies in which this situation has been assessed quantitatively. In addition, Yamashita et al.[12] found a robust positive association between the retinal nerve fiber layer and axial length and RAT. Although there is no study in which this situation has been evaluated with quantitative analysis, it is unknown what subclinical changes may occur in non-PDR or PDR and what kind of changes this situation may cause in the retinal vascular system.

As mentioned, MH and ERM represented a narrower "a" value for RAT, and VMT represented a more comprehensive "a" value for RVT. In the retina, the areas outside the arcuate are more significant than those inside the arcuate. Subclinical or clinical tractional forces that may occur in PDR can be expected to pull the vascular trajectory outward. Meanwhile, retinal arteries are thinner than veins, and more exposure to tractional forces can be expected. In our study, although there was a difference in RVT values regardless of stages, there was a significant decrease in the "a" value of RAT in all three DR groups compared to the control group, which was not parallel to RVT values.

Interestingly, positive correlations emerged between HbA1C levels, the "a" value of RAT in the left eye, and the mean RAT value specifically within the PDR cohort (r=0.737, p=0.002; r=0.669, p=0.006). Maintaining optimal glucose control throughout life, regardless of DR severity, is widely recognized as a means to mitigate the progression to PDR and the accompanying risk of vision-threatening complications, as elevated HbA1c

levels are likely correlated with the advancement to PDR.[13] Similarly, the tractional forces within the arcuate region that may occur in PDR could lead to a relative constriction in the trajectories due to their proximity to the evaluated vessel systems. However, as previously mentioned, such a change was not observed in the venous system, which is thicker than the arterial system and is expected to be more resistant to tractional forces. To address this knowledge gap, the current study employed a different methodology to investigate the effects of DR on retinal vasculature trajectory. The study aimed to elucidate the relationship between disease severity and retinal vascular morphology by analyzing fundus images from a cohort of DR patients and controls. The findings revealed asymmetric significant alterations in RAT and RVT in DR patients compared to controls, with the most pronounced changes observed in the proliferative stage of the disease. These findings suggest that curvature alterations in the RA trajectory, particularly in the proliferative phase of DR, may reflect underlying tractional changes even before overt clinical tractional signs are present. If validated in future longitudinal studies, these trajectory metrics could serve as non-invasive imaging biomarkers to monitor disease progression or predict risk for vision-threatening complications. Such quantitative imaging tools may enhance clinical decision-making in DR management.

The primary limitation of this study was the relatively small patient cohort. Subclinical or clinical tractional forces that may occur in DR may result in RA trajectory alterations that are not always accompanied by parallel changes in the RVs, although this requires further validation. In addition, the cross-sectional nature of the study precludes the establishment of causality between tractional forces and retinal vascular changes in DR. Although intra-observer reproducibility analysis was not statistically evaluated, the use of a standardized protocol by an experienced examiner helped minimize variability.[3,5,12] Future prospective studies with bigger cohorts and longitudinal follow-up are necessary to validate these findings and clarify the clinical implications of retinal vascular alterations in DR.

Conclusion

This study provides important insights into the effects of DR on retinal vasculature trajectory, highlighting the potential contribution of tractional forces to disease pathogenesis. By elucidating the relationship between disease severity, glycemic control, and retinal vascular morphology, the findings offer valuable information that may inform the development of targeted therapeutic strategies to preserve vision and reduce the burden of DR on affected individuals. Future studies should focus on prospective longitudinal designs involving larger patient cohorts and multiple trained observers to validate the reproducibility and clinical relevance of these trajectory-based metrics. Furthermore, examining the predictive value of such changes in relation to DR progression could enhance their potential utility in clinical settings.

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References

1. Four risk factors for severe visual loss in diabetic retinopathy. The third report from the Diabetic Retinopathy Study. The Diabetic Retinopathy Study Research Group. Arch Ophthalmol 1979;97:654–5. [CrossRef]
2. Klein R, Klein BE, Moss SE. Epidemiology of proliferative diabetic retinopathy. Diabetes Care 1992;15:1875–91. [CrossRef]
3. Yoshihara N, Sakamoto T, Yamashita T, Yamashita T, Yamakiri K, Sonoda S, et al. Wider retinal artery trajectories in eyes with macular hole than in fellow eyes of patients with unilateral idiopathic macular hole. PLoS One 2015;10:e0122876. [CrossRef]
4. Frank RN. Diabetic retinopathy. N Engl J Med 2004;350:48–58. [CrossRef]
5. Yucel Gencoglu A, Ağın A, Un Y, Ozturk Y. Quantification of retinal vein and artery trajectories using second-order polynomial equation in eyes with vitreomacular traction. Photodiagnosis Photodyn Ther 2023;42:103616. [CrossRef]
6. Kannel WB, D'Agostino RB, Wilson PW, Belanger AJ, Gagnon DR. Diabetes, fibrinogen, and risk of cardiovascular disease: The Framingham experience. Am Heart J 1990;120:672–6. [CrossRef]
7. Stern DM, Esposito C, Gerlach H, Gerlach M, Ryan J, Handley D, et al. Endothelium and regulation of coagulation. Diabetes Care 1991;14:160–6. [CrossRef]

8. Garner A. Histopathology of diabetic retinopathy in man. Eye (Lond) 1993;7:250–3. [CrossRef]
9. Le TN, Bright R, Truong VK, Li J, Juneja R, Vasilev K. Key biomarkers in type 2 diabetes patients: A systematic review. Diabetes Obes Metab 2025;27:7–22. [CrossRef]
10. Aiello LP, Wong JS. Role of vascular endothelial growth factor in diabetic vascular complications. Kidney Int Suppl 2000;77:S113–9. [CrossRef]
11. Ma IH, Yang CM, Hsieh YT. The correlations of macular structure characteristics with idiopathic epiretinal membrane and its sexual preference-A matched comparison study. Invest Ophthalmol Vis Sci 2022;63:10. [CrossRef]
12. Yamashita T, Sakamoto T, Terasaki H, Tanaka M, Kii Y, Nakao K. Quantification of retinal nerve fiber and retinal artery trajectories using second-order polynomial equation and its association with axial length. Invest Ophthalmol Vis Sci 2014;55:5176–82. [CrossRef]
13. Perais J, Agarwal R, Evans JR, Loveman E, Colquitt JL, Owens D, et al. Prognostic factors for the development and progression of proliferative diabetic retinopathy in people with diabetic retinopathy. Cochrane Database Syst Rev 2023;2:CD013775. [CrossRef]