## ORIGINAL RESEARCH

## Value of Doppler Ultrasonography in Assessing the Efficacy of Diabetic Retinopathy: A Retrospective Analysis

Xinming Peng, MM; Peng Chen, MM; Yiwen Liu, BM; Yajing Lv, BM; Guang Chen, MM; Jing Wang, MM

#### ABSTRACT

**Objective** • To investigate the value of Doppler ultrasound in evaluating the efficacy of diabetic retinopathy.

**Methods** • A retrospective analysis was conducted on 90 hospitalized patients with type 2 diabetes from January 2019 to January 2020. The patients were divided into two groups: 34 cases without retinopathy and 56 cases with diabetic retinopathy. Clinical data and Doppler ultrasonography results were collected and analyzed to evaluate the value of Doppler ultrasound.

**Results** • After treatment, various indicators, including blood glucose, HbA<sub>1c</sub>, FPG, 2hFPG, HOMA-IR, and FINS, showed significant improvement in both groups (P < .05). There was no significant difference before and after treatment (P > .05). Before treatment, the retinopathy group exhibited significantly different central artery parameters: PSA ( $8.35 \pm 1.08$ ), EDV ( $5.80 \pm 0.62$ ), RI ( $1.53 \pm 0.25$ ), compared to patients without retinopathy: PSA ( $13.61 \pm 1.80$ ), EDV ( $7.23 \pm 0.51$ ), RI ( $0.85 \pm 0.02$ ) (t = 12.019, 11.631, 11.461, P = .01, .01, .00), respectively. After treatment, the central artery parameters improved in both groups. The retinopathy group showed PSA ( $10.44 \pm 0.26$ ), EDV ( $6.84 \pm 0.85$ ), RI ( $1.01 \pm 0.04$ ), while patients

Xinming Peng, MM, Associate Chief Physician; Peng Chen, MM, Attending Doctor; Yajing Lv, BM, Deputy Chief Nurse; Guang Chen, MM, Associate Chief Physician; Jing Wang, MM, Attending Doctor; Department of Ophthalmology, Affiliated Hospital of Hebei University, Hebei, Baoding, China. Yiwen Liu, BM, Student, Department of Clinical Medicine, Hebei University Medical College, Hebei, Baoding, China.

Corresponding author: Xinming Peng, MM E-mail: pengxm\_2006@hbu.edu.cn

#### INTRODUCTION

Microvascular complications in diabetes are a significant cause of blindness.<sup>1</sup> It is estimated that one-third of patients with diabetes are at risk of developing cardiovascular diseases, including stroke, coronary heart disease, and heart failure.<sup>2</sup> While timely laser therapy has demonstrated effectiveness in without retinopathy exhibited PSA ( $15.13 \pm 1.20$ ), EDV (8.50 ± 0.80), RI ( $0.71 \pm 0.08$ ) (t = 15.94, 12.01, 13.32, P = .01, .01, .01), respectively. Similarly, before treatment, the retinopathy group had different central artery parameters: PSA ( $30.35 \pm 5.15$ ), EDV ( $8.85 \pm 1.67$ ), RI ( $1.53 \pm 0.25$ ), compared to patients without retinopathy: PSA ( $34.41 \pm 5.20$ ), EDV ( $11.34 \pm 2.56$ ), RI ( $0.88 \pm 0.15$ ) (t = 12.108, 11.542, 11.57, P = .01, .01, .01), respectively. After treatment, the central artery parameters improved in both groups. The retinopathy group showed PSA ( $33.26 \pm 4.27$ ), EDV ( $9.37 \pm 1.86$ ), RI ( $0.98 \pm 0.35$ ), while patients without retinopathy exhibited PSA ( $36.15 \pm 4.24$ ), EDV ( $13.51 \pm 2.13$ ), RI ( $0.76 \pm 0.23$ ) (t = 13.84, 12.14, 10.11, P = .01, .01, .01), respectively.

**Conclusions** • Color Doppler ultrasound monitoring of fundus hemodynamic parameters can accurately reflect the changes in blood vessels in diabetic eyes. It provides real-time and objective evaluation of fundus hemodynamic indexes. This technology demonstrates high repeatability and simple operation, making it valuable for the non-invasive detection of early retinopathy. (*Altern Ther Health Med.* 2023;29(6):260-263).

preserving vision in patients with proliferative retinopathy and macular edema, its capacity to reverse vision loss remains limited. In advanced cases of retinopathy, vitrectomy may be required.<sup>1,2</sup> Doppler ultrasound of the eye is a widely employed technique for evaluating various ocular conditions and has emerged as a valuable tool for diagnosing a range of eye diseases. It allows for the assessment of blood flow in the eyes and the detection of opacity in the posterior segment. Therefore, this study focuses on assessing the value of Doppler ultrasound in assessing the efficacy of diabetic retinopathy.

#### MATERIALS AND METHODS

#### **Study Design and Study Population**

The study design employed in this research was a retrospective analysis conducted from January 2019 to January 2020. A total of 90 hospitalized patients with type 2 diabetes were included. Based on the presence or absence of diabetic retinopathy, the patients were divided into two

groups: the non-retinopathy group (34 cases) and the diabetic retinopathy group (56 cases). All patients included in this study provided informed consent, and either the patients themselves or their representatives signed the necessary consent forms.

#### **Inclusion and Exclusion Criteria**

The inclusion criteria for this study were as follows: (1) clinically diagnosed type 2 diabetes mellitus; (2) with or without retinopathy; (3) normal cardiopulmonary function. Exclusion Criteria: The exclusion criteria were as follows (1) the presence of hypertension, ischemic cerebrovascular disease, coronary heart disease, glaucoma, cataract, refractive error, macular degeneration, retinal vascular occlusion, ischemic optic neuropathy, history of laser photocoagulation or ophthalmic surgery, and other microcirculation disorders; (2) Patients with combined malignant disease, mental illness, drug allergy, or any other conditions that could potentially affect ocular artery hemodynamics were also excluded.

#### Assessment of Serum Biochemical Indexes

Serum biochemical indexes were checked for all the enrolled candidates, including fasting blood glucose (FBG), glycosylated hemoglobin (HbA<sub>1c</sub>), 2-hour postprandial blood glucose (2hFPG), and insulin resistance index (HOMA-IR).

#### **Doppler Ultrasound Examination Procedure**

A GE-VIVID7 color ultrasound system (GE Company, USA) with a 4-8 MHz probe was utilized during the Doppler ultrasound examination. Simultaneously, electrocardiogram readings were recorded. Standardization was ensured by having the same operator perform all procedures under consistent conditions. Before the examination, participants refrained from smoking, drinking, or consuming tea, coffee, or other beverages. They sat for 10 minutes to stabilize their blood pressure and intraocular pressure within the normal range. The examination was conducted with the subject lying flat, gently closing their eyelids, and applying a coupling agent on the eyelid surface. The probe was positioned in contact with the upper eyelid without exerting pressure on the eyeball, and a horizontal scan was performed. Color Doppler was activated to locate the column of color blood flow in the eye artery along the optic nerve. A sampling segment with a sampling angle of <15° and the best color blood flow display was selected for measurement, with a sampling volume set at 1.0 mm  $\times$  1.0 mm. The sampling points for the central retinal artery and ophthalmic artery were located 2 mm behind the optic disc and approximately 1.5 cm behind the eyeball, respectively. Clear blood flow spectra were obtained using pulse Doppler, and the images were frozen. Measurements of peak systolic velocity (PSV) and end-diastolic velocity (EDV) were obtained for the central retinal artery (CRA) and ophthalmic artery (OA) using the Doppler method. The resistance index (RI) was calculated as an average value based on three consecutive determinations of the blood flow spectrum.

## Table 1. General Information of Patients

	Non-Retinopathy	Retinopathy	-	
Item	Group	Group	$t/\chi^2$	P value
Case	34	56		
Age	$56.51 \pm 6.36$	$58.25 \pm 5.14$	1.81	.07
Gender			0.20	.65
Male	20	30		
Female	14	26		
Nationality			2.12	.08
Han Nationality	31	54		
Others	3	0		
Do You Have Any			0.21	.65
Previous Eye Disease?				
Yes	0	0		
No	34	56		

**Note:** *t* represents the *t* test,  $\chi^2$  represents the chi-square test

#### **Observation indicators**

The observation included a comparison of various serum biochemical indicators, such as FBG, HbA<sub>1c</sub>, 2hFPG, and HOMA-IR. Additionally, measurements of maximum systolic PSV, EDV, and RI were obtained for the central artery and ophthalmic artery.

## **Statistical Analysis**

The data obtained in this study were analyzed using the Statistical Product and Service Solutions (SPSS) 21.0 software package (IBM, Armonk, NY, USA). Categorical variables were tested using the  $\chi^2$  test (%), while continuous variables were assessed using the *t* test ( $\overline{x \pm s}$ ). A significance level of *P*<.05 was considered to indicate statistical significance.

## RESULTS

## **Baseline Data Comparison of Patients**

A total of 90 eligible patients were included in the study, with 34 patients without retinopathy and 56 patients with diabetic retinopathy. There were no significant differences in terms of gender, age, and past medical history between the two groups (P > .05 for all comparisons). Table 1 presents the general characteristics of the patients included in this study.

# Blood Glucose Indices Before and After Treatment in Diabetic Patients

The comparison of various indicators between the two groups of patients revealed a significant improvement in blood glucose levels and other parameters (HbA<sub>1c</sub>, FPG, 2hFPG, HOMA-IR, and FINS) after treatment compared to before treatment (P<.05). However, no significant difference was observed between the before and after treatment values (P>.05). Detailed information can be found in Table 2.

## Comparison of Central Artery CRA-Related Indicators

Before treatment, significant differences were observed in the central artery peak systolic velocity (PSA)  $(8.35 \pm 1.08 \text{ vs.} 13.61 \pm 1.80)$ , end-diastolic velocity (EDV)  $(5.80 \pm 0.62 \text{ vs.} 7.23 \pm 0.51)$ , and resistance index (RI)  $(1.53 \pm 0.25 \text{ vs.} 0.85 \pm 0.02)$  between the retinopathy and non-retinopathy groups **Table 2.** Comparison of Various Indicators Between the Two Groups  $(\overline{x \pm s})$ 

		HbA <sub>16</sub> (%)		FPG (mmol/L)		2hFPG (mmol/L)		HOMA-IR	
		Before	After	Before	After	Before	After	Before	After
Group	Cases	Therapy	Treatment	Therapy	Treatment	Therapy	Treatment	Therapy	Treatment
Retinopathy Group	56	$8.32 \pm 1.42$	$5.37 \pm 0.52$	9.31 ± 1.22	$4.89 \pm 0.74$	$15.94 \pm 3.04$	$5.92 \pm 1.41$	$2.41 \pm 1.23$	$1.31 \pm 0.64$
Non-Retinopathy Group	34	$8.47 \pm 1.22$	5.73 ± 0.86	$9.24 \pm 1.36^{\text{a}}$	$4.51 \pm 0.63^{a}$	$16.05 \pm 2.96^{a}$	$5.61 \pm 1.83^{\text{a}}$	$2.42 \pm 1.41^{a}$	$1.42 \pm 0.83^{a}$
t		1.39	1.08	1.97	1.07	1.25	1.98	1.46	1.39
P value		.02	.21	.12	.06	.21	.15	.05	.31

<sup>a</sup>*P*<.05 indicates a significant difference between before therapy and after treatment within the non-retinopathy group.

Note: Data presented as mean  $\pm$  standard deviation ( $\overline{x} \pm s$ ). The *t* test was used for statistical analysis.

(t = 12.02, 11.63, 11.46, P = .01, .01, .01). After treatment, improvements were observed in the central artery PSA (10.44 ± 0.26 vs. 15.13 ± 1.20), EDV (6.84 ± 0.85 vs. 8.50 ± 0.80), and RI (1.01 ± 0.04 vs. 0.71 ± 0.08) in the two groups, with significant differences noted (t = 15.94, 12.01, 13.33, P = .01, .01, .01). Refer to Table 3 for detailed information.

## Comparison of Ophthalmic Artery (OA) Related Indexes

Before treatment, significant differences were observed in the ophthalmic artery peak systolic velocity (PSA)  $(30.35 \pm 5.15 \text{ vs.})$  $34.41 \pm 5.20$ ), end-diastolic velocity (EDV) (8.85±1.67 vs. 11.34±2.56), and resistance index (RI) (1.53  $\pm$ 0.25 vs.  $0.88 \pm 0.15$ ) between the retinopathy and non-retinopathy groups (t = 12.11, 11.54, 11.57, P = .01, .01, .00). After treatment, improvements were observed in the ophthalmic artery PSA ( $33.26 \pm$ 4.27 vs. 36.15 ± 4.24), EDV (9.37 ± 1.86 vs. 13.51 ± 2.13), and RI (0.98 ± 0.35 vs.  $0.76 \pm 0.23$ ) in the two groups, with significant differences noted (t = 13.84, 12.14, 10.11,*P*=.01, .01, .01). Refer to Table 4 for detailed results.

## DISCUSSION

Common ocular complications in diabetes include diabetic retinal

disease and early cataracts, which can ultimately result in blindness.<sup>3</sup> Despite the effectiveness of diabetic retinopathy treatment, it remains the leading cause of blindness among working-age individuals in industrialized countries.<sup>4</sup> Vision loss can occur in the macula, the central part of the retina, due to factors such as intraretinal hemorrhage, macular edema, traction retinal detachment, or capillary loss in the peripheral

**Table 3.** Comparison of Central Artery CRA-Related Indicators Between the Two Groups of Patients  $(x \pm s)$ 

	PSA		EI	OV	RI		
	Before	After	Before	After	Before	After	
Group	Therapy	Treatment	Therapy	Treatment	Therapy	Treatment	
Retinopathy Group	8.35 ± 1.08	$10.44 \pm 0.26$	$5.80 \pm 0.62$	6.84±0.85	1.53±0.25	$1.01 \pm 0.04$	
Non-Retinopathy Group	$13.61 \pm 1.80^{**}$	15.13±1.20ª	$7.23 \pm 0.51^{a}$	$8.50 \pm 0.80^{a}$	$0.85 \pm 0.02^{\circ}$	$0.71 \pm 0.08^{\mathrm{b}}$	
t	12.02	15.94	11.63	12.06	11.46	13.33	
P value	.01	.01	.01	.01	.01	.01	
<sup>a</sup> P<.05							

<sup>&</sup>lt;sup>b</sup>*P* < .01

Note: *P* values indicate significant differences between the retinopathy and non-retinopathy groups.

**Abbreviations**:  $(\overline{x \pm s})$ , mean  $\pm$  standard deviation; *t*: *t* test; PSA, Peak Systolic Velocity; EDV, End Diastolic Velocity; RI, Resistance Index.

**Table 4.** Comparison of Central Artery CRA-Related Indicators Between the Two Groups  $(\overline{x} \pm s)$ 

	PS	A	EL	ov	RI		
Before		After	Before	After	Before	After	
Group	Therapy	Treatment	Therapy	Treatment	Therapy	Treatment	
Retinopathy Group	$30.35 \pm 5.15$	$33.26 \pm 4.27$	$8.85 \pm 1.67$	$9.37 \pm 1.86$	$1.18 \pm 0.31$	$0.98 \pm 0.35$	
Non-Retinopathy Group	$34.41 \pm 5.20^{a}$	$36.15\pm4.24^{\text{a}}$	$11.34 \pm 2.56^{b}$	$13.51 \pm 2.13^{b}$	$0.88\pm0.15^{\text{a}}$	$0.76 \pm 0.23^{b}$	
t	12.11	13.84	11.54	12.14	11.57	10.11	
P value	.01	.01	.01	.01	.00	.01	

 $^{a}P < .05$  $^{b}P < .01$ 

Note: *P* values indicate significant differences between the retinopathy and non-retinopathy groups. Data presented as mean  $\pm$  standard deviation ( $\overline{x \pm s}$ ).

**Abbreviations**: PSA, Peak Systolic Velocity; EDV, End Diastolic Velocity; RI, Resistance Index.

annulus. Regular preventive eye examinations and timely treatment can help prevent vision loss.<sup>3,4</sup>

Chronic hyperglycemia can result in dysfunction and damage to various organs, with vascular lesions being a common late complication of diabetes. Microvascular lesions can affect the eyes, kidneys, and nervous system, while macrovascular disease involves coronary and peripheral vessels.<sup>5,6</sup> Diabetic

<sup>&</sup>lt;sup>c</sup>P<.001

retinopathy, characterized by retinal vessel closure and increased permeability, is the most prevalent microvascular complication. The exact pathological mechanisms underlying the development and progression of diabetic retinopathy are still not fully understood, despite extensive research. Diagnostic tests for diabetic retinopathy typically involve imaging eyeball and retinal blood vessels, including fluorescein angiography, retinal optical coherence tomography, B-mode ultrasound imaging, perimetry, and digital retinal photography.<sup>7</sup>

Several studies have explored the relationship between changes in retrobulbar circulation and the progression of diabetic retinopathy using Doppler ultrasound. Color Doppler imaging, a non-invasive technique, allows for measuring blood flow velocity in the small blood vessels of the eye. Typically, the ophthalmic artery, which is the primary branch of the internal carotid artery, as well as the central retinal veins and arteries and the posterior ciliary artery, are the vessels most commonly evaluated.<sup>7-9</sup>

Analyzing retrobulbar vascular hemodynamic changes can offer valuable insights into the diabetic process and help address whether there is a correlation between the progression of diabetic retinopathy and observed alterations in ocular vascular blood flow. Diabetic retinopathy, a severe form of microvascular disease associated with diabetes, is characterized by symptoms such as blurred vision or double vision and is a prevalent cause of blindness.<sup>10-12</sup>

Patients with diabetic retinopathy experience irreversible vision changes following noticeable fundus alterations, and currently, no effective treatment is available to reverse or prevent them. Therefore, a simple, cost-effective method is highly valuable for early diagnosis, treatment, and vision improvement in diabetic retinopathy. The changes in retinal blood vessels are closely associated with retinal ischemia, characterized by thickening of the microvessels' basal cell wall, microaneurysms, increased vascular permeability, and retinal surface vascular malformations, as well as reduced retinal blood flow. Evidence suggests that retinal microcirculation changes occur prior to morphological alterations.<sup>13-15</sup>

The central retinal artery originates from the blood vessels at the posterior part of the retina, and its hemodynamic changes directly influence the blood supply to the retina. On the other hand, the ophthalmic artery originates from the carotid artery and supplies blood to the structures surrounding the eye, including the choroid. Any disturbances in the retinal and choroidal microcirculation can lead to hemodynamic changes in the OA, and damage to the choroid can further exacerbate microcirculatory issues. Alterations in blood flow within the CRA and OA directly impact retinal microcirculation, and measuring these indicators can provide valuable insights into the blood supply status of the retina and optic disc.

#### **Study Limitations**

There are a few limitations to be considered in this study. Firstly, the study design was retrospective, which may introduce potential bias and limit the ability to establish causal relationships. Secondly, the sample size was relatively small, which could affect the generalizability of the findings to a larger population. Additionally, the study focused on a specific timeframe and a single healthcare facility, which may limit the external validity of the results. Moreover, the reliance on selfreporting or medical records for data collection introduces the possibility of information bias. Finally, the study did not account for potential confounding variables, such as comorbidities or medication use, which could impact the observed outcomes. These limitations should be considered when interpreting the findings; further research is needed to overcome these limitations and provide more robust evidence.

#### CONCLUSION

In conclusion, color Doppler ultrasound proves to be a valuable tool for monitoring hemodynamic parameters of fundus blood vessels, evaluating blood flow circulation, and detecting early retinal and choroidal lesions in a direct, objective, and accurate manner. Its strong repeatability and ease of use make it an important non-invasive method for early detection of retinal lesions. Therefore, the clinical promotion and application of color Doppler ultrasound are highly recommended.

#### CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

#### AUTHOR CONTRIBUTIONS

XP and PC designed the study and performed the experiments, YLiu and YLv collected the data, GC and JW analyzed the data, XP and PC prepared the manuscript. All authors read and approved the final manuscript. XP and PC contributed equally to this study as co-first authors.

#### FUNDING

This study was supported by the Baoding Science and technology planning project (2141ZF308).

#### REFERENCES

- Castilla-Guerra L, Gómez Escobar A, Gómez Cerezo JF. Utility of Doppler ultrasound for the study of ocular vascular disease. *Rev Clin Esp (Barc)*. 2021;221(7):418-425. doi:10.1016/j.rceng.2020.11.007
- Pauk-Domańska M, Walasik-Szemplińska D. Color Doppler imaging of the retrobulbar vessels in diabetic retinopathy. J Ultrason. 2014;14(56):28-35. doi:10.15557/JoU.2014.0003
- de Fátima Ribeiro Dos Anjos G, de Freitas MAR, Dos Santos MCA, Diniz ALD. Doppler Indices of the Ophthalmic Artery in Pregnant Women With Pregestational Diabetes Mellitus With and Without Retinopathy. J Ultrasound Med. 2021;40(2):251-257. doi:10.1002/jum.15393
- Hartenstein S, Müller B, Metze B, Czernik C, Bührer C. Blood flow assessed by color Doppler imaging in retinopathy of prematurity. J Perinatol. 2015;35(9):745-747. doi:10.1038/jp.2015.45
- Kollias AN, Ulbig MW. Diabetic retinopathy: early diagnosis and effective treatment. Dtsch Arztebl Int. 2010;107(5):75-83. doi:10.3238/arztebl.2010.0075
- Bandello F, Cicinelli MV. 19th EURETINA Congress Keynote Lecture: Diabetic Retinopathy Today. Ophthalmologica. 2020;243(3):163-171. doi:10.1159/000506312
- Dimitrova G, Kato S. Color Doppler imaging of retinal diseases. Surv Ophthalmol. 2010;55(3):193-214. doi:10.1016/j.survophthal.2009.06.010
- Yilmaz Ovali G, Ersoy B, Tuncyurek O, et al. Doppler ultrasonography imaging of hemodynamic alteration of retrobulbar circulation in type 1 diabetic children and adolescents without retinopathy. *Diabetes Res Clin Pract.* 2008;79(2):243-248. doi:10.1016/j.diabres.2007.09.001
- Lin KY, Hsih WH, Lin YB, Wen CY, Chang TJ. Update in the epidemiology, risk factors, screening, and treatment of diabetic retinopathy. J Diabetes Investig. 2021;12(8):1322-1325. doi:10.1111/jdi.13480
- Bittner M, Faes L, Boehni SC, Bachmann LM, Schlingemann RO, Schmid MK. Colour Doppler analysis of ophthalmic vessels in the diagnosis of carotic artery and retinal vein occlusion, diabetic retinopathy and glaucomac systematic review of test accuracy studies. *BMC Ophthalmol.* 2016;16(1):214. doi:10.1186/s12886-016-0384-0
- Chaudhary S, Zaveri J, Becker N. Proliferative diabetic retinopathy (PDR). Dis Mon. 2021;67(5):101140. doi:10.1016/j.disamonth.2021.101140
- Lechner J, O'Leary OE, Stitt AW. The pathology associated with diabetic retinopathy. Vision Res. 2017;139:7-14. doi:10.1016/j.visres.2017.04.003
- Karami M, Janghorbani M, Dehghani A, Khaksar K, Kaviani A. Orbital Doppler evaluation of blood flow velocities in patients with diabetic retinopathy. *Rev Diabet Stud.* 2012;9(2-3):104–111. doi:10.1900/RDS.2012.9.104
- Meng N, Liu J, Zhang Y, Ma J, Li H, Qu Y. Color Doppler Imaging Analysis of Retrobulbar Blood Flow Velocities in Diabetic Patients Without or With Retinopathy: A Meta-analysis. J Ultrasound Med. 2014;33(8):1381-1389. doi:10.7863/ultra.33.8.1381
- MacKinnon JR, McKillop G, O'Brien C, Swa K, Butt Z, Nelson P. Colour Doppler imaging of the ocular circulation in diabetic retinopathy. *Acta Ophthalmol Scand.* 2000;78(4):386-389. doi:10.1034/j.1600-0420.2000.078004386.x