https://doi.org/10.46389/rjd-2022-1073
www.rjdnmd.org

Rom J Diabetes Nutr Metab Dis
2022; volume 29, issue 1, pages 40–49

Original Research

Trans-cranial duplex and visfatin as markers for cerebrovascular complications in type 2 diabetes mellitus

Ssamaa Ayman[1], Sahar Nassef[1], Nagwa Ramadan[2], Dina Sabry[3,4], Kareem Mohsen Moussa[5], Ahmed Fayed[6,*]

[1] Vascular Medicine Unit, Internal Medicine Department, Kasr Alainy School of Medicine, Cairo University, Egypt
[2] Endocrinology Unit, Internal Medicine Department, Kasr Alainy School of Medicine, Cairo University, Egypt
[3] Medical Biochemistry and Molecular Biology Department, Kasr Alainy School of Medicine, Cairo University, Egypt
[4] Medical Biochemistry and Molecular Biology Department, Badr University in Cairo, Egypt
[5] Radiodiagnosis Department, Internal Medicine Department, Kasr Alainy School of Medicine, Cairo University, Egypt
[6] Nephrology Unit, Internal Medicine Department, Kasr Alainy School of Medicine, Cairo University, Egypt

*Correspondence to: Ahmed Fayed, Cairo University Hospitals, Al-Saray St., El-Maniel, 11562, Cairo, Egypt, Phone: +201142700904, E-mail: Dr.fayed@gmail.com

Received: 2 July 2021 / Accepted: 16 August 2021

Abstract

Background and aims: Transcranial doppler (TCD) is a modern and sophisticated diagnostic procedure that enables recording the changes in cerebral perfusion in various states. We aimed to look into the role of TCD in studying the cerebral changes that occur in type 2 diabetic patients, as well as their relationship to visfatin and macro-and microvascular complications. **Material and method:** Twenty diabetic patients with no vascular complications were placed in group1, twenty diabetic patients with macrovascular complications were placed in group 2, and forty diabetic patients with microvascular complications were placed in group 3. Serum visfatin level and TCD were performed on all patients. **Results:** The pulsatile index of the right and left middle cerebral arteries (PI RT and LT MCA) have high sensitivity (69.2% and 64.1%, respectively) and specificity (75% and 95%) in predicting microvascular complications, with cut-off values of (1.005 and 1.035). A positive significant correlation between serum visfatin level and PI RT, and LT MCA with ($p<0.001$, =0.035. respectively) among diabetics with no complications group, ($p<0.001$) in both macro and micro-vascular complications group. **Conclusion:** TCD is a non-invasive technique for determining brain circulation and predicting complications and prognosis in high-risk diabetics.

Keywords: type 2 diabetes mellitus, transcranial doppler, visfatin, microvascular complications, macro-vascular complications.

Background and aims

Diabetes mellitus (DM) is a group of metabolic disorders caused by a lack of insulin in a person's blood or a problem with their body's ability to use the insulin it generates (insulin resistance) [1]. Type 2 diabetes mellitus (T2DM) is a leading cause of severe morbidities and disabilities (blindness, chronic renal impairment, cardiovascular events, and lower limb amputation) [2]. As a result, DM is linked to 2-fold increased risk of stroke, with about 1 in 5 DM patients dying from a stroke [3].

Visfatin, also known as nicotinamide phosphoribosyltransferase (NAMPT) and

pre-B-cell colony-enhancing factor, is a ubiquitous intracellular enzyme (PBEF-1). It's also been labeled as a new adipocytokine [4]. It is formed primarily in visceral adipose tissue and is also expressed in isolated subcutaneous adipose cells. Visfatin is an insulin-like substance that reduces blood glucose levels [5]. Plasma visfatin has been linked to a variety of metabolic states in studies. Obesity, type 2 diabetes, metabolic syndrome, and cardiovascular disorders were all linked to an increase in it [6].

TCD is a simple and non-invasive method for detecting intracranial arterial abnormalities, especially steno-occlusive lesions. When it's associated with a microvascular complication like retinopathy, neuropathy, or nephropathy, the increase is even more pronounced [7].

We aimed to look into the role of TCD in studying the cerebral changes that occur in type 2 diabetic patients, as well as their relationship to visfatin and macro-and microvascular complications.

Material and method

From November 2017 to March 2020, 80 diabetic patients were collected consecutively from the Internal Medicine Department's outpatient clinic at Kasr Alainy Hospital. The WHO classification is used to diagnose diabetes. To be included in our research, participants had to have had type 2 diabetes for at least 5 years. Twenty diabetic patients with no vascular complications were placed in group 1, twenty diabetic patients with macrovascular complications were placed in group 2, and forty diabetic patients with microvascular complications were placed in group 3. Patients with a history of MRI or CT-proven stroke, as well as those with impaired kidney function, as measured by a serum creatinine level of more than 2 mg/dl, were excluded. Written consent was obtained from each patient or the patient's next of kin. All procedures carried out in this study involving human subjects adopted the ethical principles of the institutional and/or national research committee and the Helsinki Declaration of 1964 and its corresponding modifications or equivalent ethical standards. This work was accepted by the Local Ethical Committee of Cairo University's School of Medicine's Internal Medicine department.

A detailed clinical history, complete physical examination, and Fundus examination were performed on all patients. Laboratory investigations included fasting blood sugar (FBS), 2 hours postprandial blood sugar (PPBS), lipid profile, serum creatinine, HbA_{1c}, A/C ratio, and serum visfatin level. Quantikine® ELISA kits were used to determine the amount of serum visfatin. The quantitative sandwich enzyme immunoassay technique is used in this assay. TCD was performed on all patients, and MRI brain was performed on some of them. The VasoGuard system was used to measure the peripheral arterial affection by calculating the Ankle Brachial Index (ABI), carotid Intima-Media Thickness (cIMT).

Statistical analysis

The statistical package for the social sciences (SPSS) version 26 was used to code and enter the data (IBM Corp., Armonk, NY, USA). In quantitative data, mean, standard deviation, median, minimum, and maximum were used, while categorical data were summarized using frequency (count) and relative frequency (percentage). The non-parametric Kruskal-Wallis and Mann-Whitney tests were used to compare quantitative variables [8]. The Chi-square ($\chi 2$) test was used to compare categorical results. When the predicted frequency is less than 5, an exact test was used instead [9]. The Spearman correlation coefficient was used to determine correlations between quantitative variables [10]. The best cut-off value of significant parameters for detecting complications was determined using a ROC curve and region under the curve analysis. Statistical significance was described as a p-value of less than 0.05.

Results

Table 1 summarizes the demographic and laboratory data of the groups examined. The level of serum visfatin was higher in diabetic patients

Table 1: Demographic and laboratory data in studied groups. *p<0.05 are significantly different.

Variables	Group I diabetic with no complications [20]	Group II diabetic with macrovascular complications [20]	Group III diabetic with microvascular complications [40]	p-Value
Age (Years) (Mean±SD)	51.4±6	54.6±5	52.95±5	0.223
Male (number (%))	11 (55)	12 (60)	13 (32.5)	0.096
Female (number (%))	9 (45)	8 (40)	27 (67.5)	
Duration of DM (Years) (Mean±SD)	4.15±5	9.41±5.29	11.64±6.38	<0.001*
Presence of ischemic heart disease (number (%))	0 (0)	19 (95)	0 (0)	<0.001*
Presence of peripheral arterial disease (number (%))	0 (0)	1 (5)	0 (0)	0.519
Fundus examination				
NPDR (number (%))	0 (0)	5 (25)	23 (57.5)	<0.001*
PDR (number (%))	0 (0)	2 (10)	12 (30)	
Common carotid artery plaque				
Right CCA plaque (number (%))	0 (0)	2 (10)	3 (7.5)	0.589
Left CCA plaque (number (%))	0 (0)	3 (15)	1 (2.5)	0.130
Laboratory data (Mean±SD)				
Urea, mg/dl	28.17±13	50.23±30.7	51.87±32.64	0.001*
Creatinine, mg/dl	0.9±0.2	1.15±0.42	1.17±0.38	0.016*
Total cholesterol, mg/dl	122.35±53.1	164.05±55.95	178.21±65.87	0.003*
Triglycerides, mg/dl	83.85±55.13	127.55±72.75	146.26±86.4	<0.001*
Albumin/creatinine ratio	14.65±6.22	40±37.27	97.18±96.62	<0.001*
HbA_{1c}, %	7.74±0.64	8.68±0.86	8.64±0.88	<0.001*
Serum visfatin, mg/l	0.54±0.33	0.81±0.56	0.89±0.56	0.084
Trans cranial duplex findings				
PI RT MCA	0.91±0.22	1.10±0.25	1.10±0.19	0.005*
PI LT MCA	0.84±0.13	1.10±0.21	1.10±0.19	<0.001*
PI BA	0.85±0.18	1.02±0.22	0.99±0.18	0.01*

CCA: common carotid artery, DM: diabetes mellitus, HbA_{1c}: glycated hemoglobin, NPDR: non-proliferative diabetic retinopathy, PDR: proliferative diabetic retinopathy, PI RT MCA: pulsatile index of right middle cerebral artery, PI LT MCA: pulsatile index of left middle cerebral artery, PI BA: pulsatile index of basilar artery.

with macro and microvascular complications than in those without complications, but the difference was not statistically important (Table 1). Only the pulsatile index of the right and left middle cerebral arteries (PI RT MCA, PI LT MCA) and the pulsatile index of the basilar artery (PI BA) between the studied groups were statistically significant (Table 1).

The difference in serum creatinine level between group 1 and those with microvascular complications in group 3 was statistically significant, while the difference in HA1c level, PI LT MCA, and PI BA between group 1 and those with microvascular and macrovascular complications in groups 2 and 3 was statistically significant (Figure 1).

In group 1, there was a statistically significant association between cIMT versus patient age and creatinine level, PI RT MCA, PI LT MCA,

https://doi.org/10.46389/rjd-2022-1073

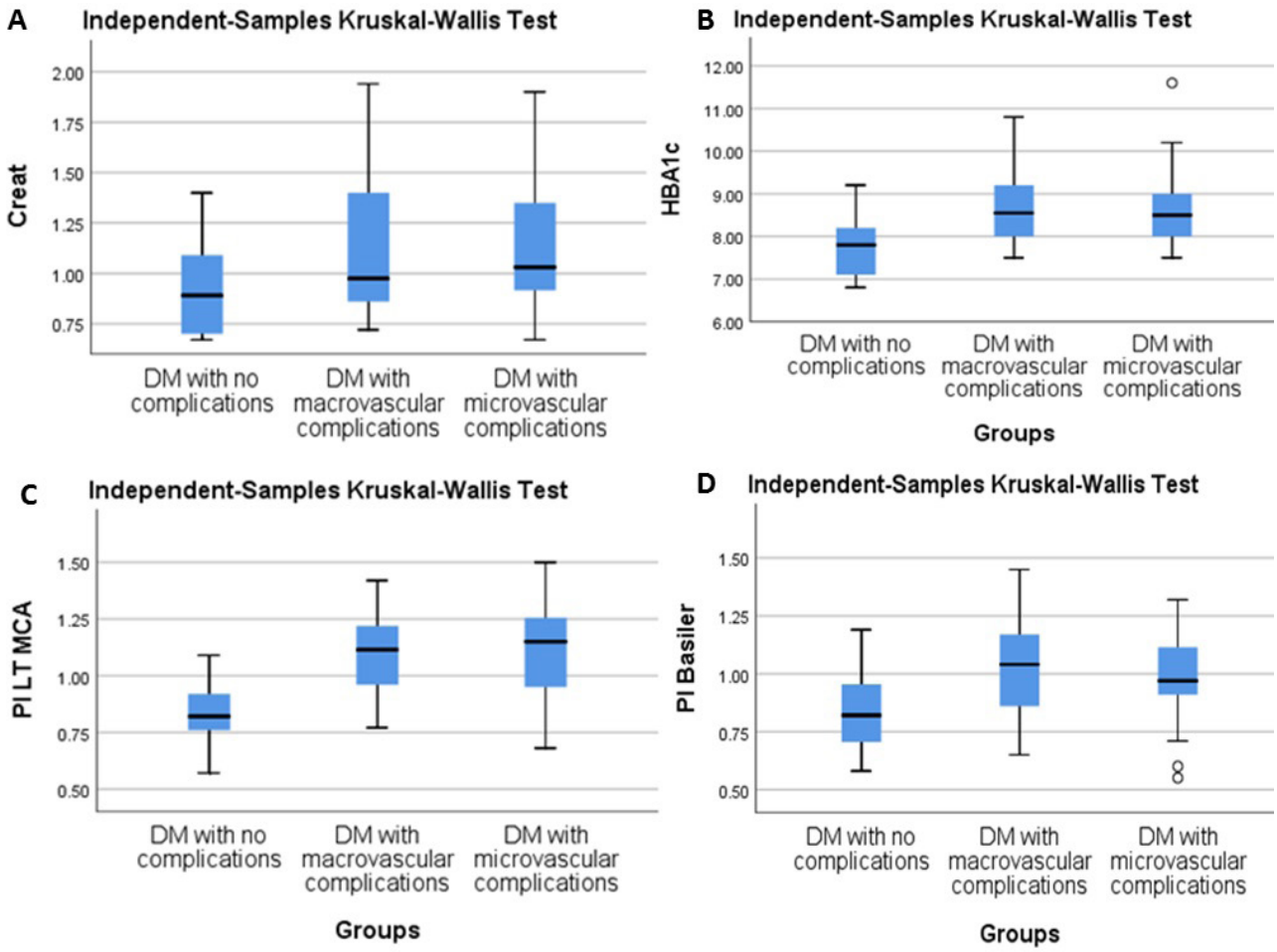


Figure 1: Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis test.
Plan A: Comparison of between studied groups regarding serum creatinine level.
Plan B: Comparison of between studied groups regarding glycated hemoglobin level.
Plan C: Comparison between studied groups regarding PI LT MCA.
Plan D: Comparison between studied groups regarding PI BA.
Creat: serum creatinine level, HbA_{1c}: glycated hemoglobin, PI LT MCA: pulsatile index of a left middle cerebral artery, PI BA: pulsatile index of the basilar artery.

and PI BA basilar versus cholesterol, and PI RT MCA, PI LT MCA, and PI BA basilar versus cholesterol. There was also a strong positive correlation between ABI and HBA_{1c} (Table 2). There was a statistically significant positive correlation between cIMT versus HBA_{1c} level, PI RT MCA, PI LT MCA, and PI BA versus HBA_{1c} level in group 2. (Table 2). In group 3, there was a statistically significant positive correlation between cIMT versus age and HBA_{1c} level, as well as a significant positive correlation between PI RT MCA and PI LT MCA versus HBA_{1c} and ABI versus HBA_{1c} (Table 2).

In all of the groups analyzed, there was a statistically significant positive correlation between serum visfatin and HA_{1c}. Serum visfatin had a statistically significant positive correlation with PI RT MCA, PI LT MCA, PI BA, and ABI (Table 3).

ROC curves were generated using PI RT MCA and PI LT MCA to predict macrovascular and microvascular complications (Figures 2 and 3). Figure 2 shows that, with cut-off values of 1.005 and1.045, PI RT and LT MCA have high sensitivity (72.7%) and specificity (75% and 95%) in the prediction of macro-vascular complications. Figure 3 shows that with a cut-off value of 1.005 and1.035, PI RT and LT MCA have high sensitivity (69.2% and 64.1%, respectively) and specificity (75% and 95%) in the prediction of microvascular complications.

Table 2: Correlations between serum duplex data with age, duration of DM and laboratory data in studied groups using Spearman correlation coefficient *p<0.05 are significantly different.

Duplex dta	Group I diabetic with no complications [20]		Group II diabetic with macrovascular complications [20]		Group III diabetic with microvascular complications [40]	
	r	p-Value	r	p-Value	r	p-Value
			Age (years)			
IMT	0.447	0.048*	0.164	0.466	0.280	0.084
ABI	-0.195-	0.409	-0.008-	0.971	-0.022-	0.896
PI RT MCA	-0.117-	0.623	0.31	0.161	0.280	0.084
PI LT MCA	-0.139-	0.56	0.327	0.137	0.077	0.643
PI BA	-0.420-	0.065	0.023	0.919	0.061	0.713
Duplex data			Duration of DM (years)			
IMT	-0.050-	0.833	0.159	0.481	0.215	0.190
ABI	0.146	0.54	0.224	0.17	-0.074-	0.655
PI RT MCA	0.127	0.594	0.808	0.117	-0.112-	0.498
PI LT MCA	0.104	0.663	0.251	0.26	-0.091-	0.580
PI BA	-0.035-	0.884	0.020	0.93	-0.249-	0.127
Duplex data			Creatinine, mg/dl			
IMT	0.629	0.003*	0.170	0.451	0.185	0.259
ABI	0.088	0.711	0.115	0.61	-0.136-	0.408
PI RT MCA	0.092	0.698	0.417	0.053	-0.097-	0.556
PI LT MCA	0.208	0.378	0.214	0.338	-0.021-	0.9
PI BA	0.098	0.68	-0.023-	0.917	-0.349-	0.029*
Duplex data			Total Cholesterol, mg/dl			
IMT	0.091	0.702	0.161	0.474	0.307	0.057
ABI	0.346	0.135	0.020	0.928	0.024	0.885
PI RT MCA	0.446	0.049*	-0.448-	0.037*	0.114	0.491
PI LT MCA	0.455	0.044*	-0.505-	0.017*	0.18	0.272
PI BA	0.459	0.042*	-0.136-	0.545	-0.250-	0.125
Duplex data			Triglycerides, mg/dl			
IMT	0.347	0.134	0.265	0.234	0.255	0.118
ABI	0.403	0.078	0.082	0.718	0.16	0.332
PI RT MCA	0.209	0.376	0.114	0.614	-0.003-	0.986
PI LT MCA	0.311	0.183	0.059	0.796	0.118	0.474
PI BA	0.181	0.446	0.280	0.207	-0.082-	0.618
Duplex data			HbA_{1c}, %			
IMT	0.243	0.301	0.573	0.005*	0.634	<0.001*
ABI	0.502	0.024*	0.389	0.074	0.428	0.007*
PI RT MCA	0.105	0.659	0.747	<0.001*	0.435	0.006*
PI LT MCA	0	0.999	0.508	0.016*	0.490	0.002*
PI BA	-0.163-	0.493	0.554	0.007*	0.154	0.349

(Continues)

https://doi.org/10.46389/rjd-2022-1073

Table 2: Continued

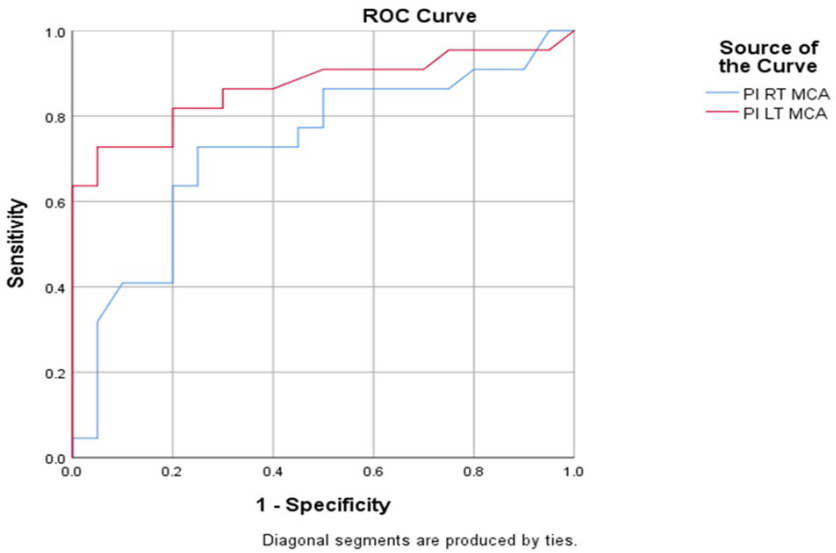
Duplex dta	Group I diabetic with no complications [20]		Group II diabetic with macrovascular complications [20]		Group III diabetic with microvascular complications [40]	
	r	p-Value	r	p-Value	r	p-Value
Duplex data			Albumin/creatinine ratio			
IMT	0.045	0.851	0.025	0.910	0.231	0.158
ABI	0.021	0.930	0.2	0.222	0.079	0.633
PI RT MCA	-0.066-	0.782	0.305	0.167	0.004	0.981
PI LT MCA	-0.017-	0.945	-0.001-	0.998	0.045	0.787
PI BA	-0.125-	0.599	0.133	0.554	-0.032-	0.846

DM: diabetes mellitus, HbA_{1c}: glycated hemoglobin, IMT: intima media thickness, ABI: ankle brachial index, PI RT MCA: pulsatile index of right middle cerebral artery, PI LT MCA: pulsatile index of left middle cerebral artery, PI BA: pulsatile index of basilar artery.

Table 3: Correlations between serum visfatin level with duplex data, age, duration of DM and laboratory data in studied groups using Spearman correlation coefficient *p<0.05 are significantly different.

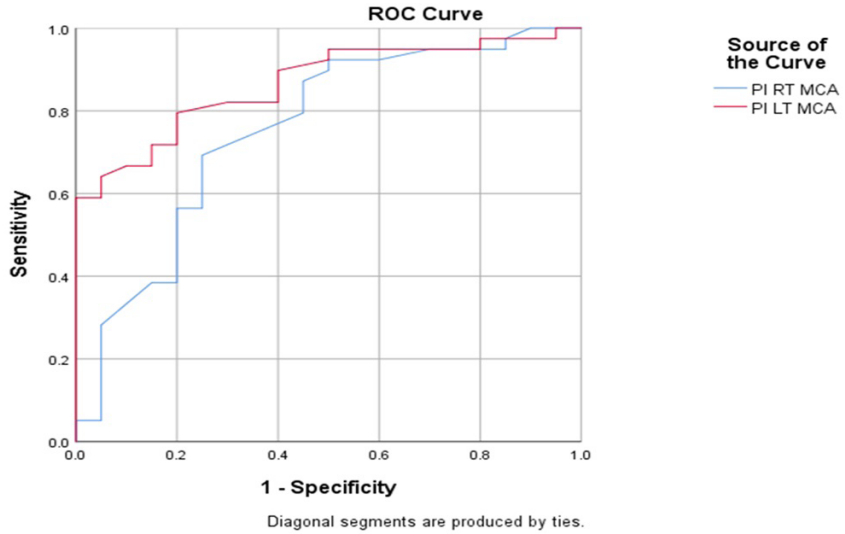
Variables	Group I diabetic with no complications [20]		Group II diabetic with macrovascular complications [20]		Group III diabetic with microvascular complications [40]	
	R	p-Value	r	p-Value	r	p-Value
			Serum visfatin level			
Age (years)	0.075	0.752	0.185	0.41	0.164	0.318
Duration of DM (years)	0.103	0.667	–0.007-	0.975	0.044	0.792
Laboratory data			Serum visfatin level			
Urea, mg/dl	0.369	0.109	0.218	0.329	-0.091-	0.581
Creatinine, mg/dl	0.322	0.166	–0.013-	0.954	-0.127-	0.44
Total cholesterol, mg/dl	0.435	0.055	-0.181-	0.419	0.177	0.282
Triglycerides, mg/dl	0.657	0.002*	0.322	0.144	0.205	0.211
Albumin/creatinine ratio	0.441	0.051	0.213	0.341	-0.142-	0.389
HbA_{1c}, %	0.609	0.004*	0.693	<0.001*	0.444	0.005*
Duplex data			Serum visfatin level			
IMT	0.404	0.077	0.224	0.315	0.148	0.368
PI RT MCA	0.713	<0.001*	0.825	<0.001*	0.745	<0.001*
PI LT MCA	0.473	0.035*	0.765	<0.001*	0.751	<0.001*
PI BA	0.487	0.03*	0.794	<0.001*	0.626	<0.001*
ABI	0.451	0.046*	0.631	0.002*	0.631	<0.001*
IMT	0.404	0.077	0.224	0.315	0.148	0.368

DM: diabetes mellitus, HbA_{1c}: glycated hemoglobin, IMT: intima media thickness, ABI: ankle brachial index, PI RT MCA: pulsatile index of right middle cerebral artery, PI LT MCA: pulsatile index of left middle cerebral artery, PI BA: pulsatile index of basilar artery.



Duplex data	AUC	P value	95% CI	Cut off	Sensitivity %	Specificity %
PI RT MCA	0.726	0.012 *	0.568 - 0.884	1.005	72.7	75
PI LT MCA	0.866	< 0.001*	0.749 - 0.983	1.045	72.7	95

Figure 2: ROC curve for prediction of macro-vascular complications using PI RT MCA, PI LT MCA. *p<0.05 are significantly different.
PI RT MCA: pulsatile index of a right middle cerebral artery, PI LT MCA: pulsatile index of a left middle cerebral artery, AUC: area under the curve, 95% CI: 95% confidence interval.



Duplex data	AUC	P value	95% CI	Cut off	Sensitivity %	Specificity %
PI RT MCA	0.754	0.002 *	0.617 - 0.891	1.005	69.2	75
PI LT MCA	0.866	< 0.001*	0.776 - 0.956	1.035	64.1	95

Figure 3: ROC curve for prediction of microvascular complications using PI RT MCA, PI LT MCA. *p<0.05 are significantly different.
PI RT MCA: pulsatile index of a right middle cerebral artery, PI LT MCA: pulsatile index of a left middle cerebral artery, AUC: area under the curve, 95% CI: 95% confidence interval.

Discussion

Endothelial dysfunction and a decrease in endothelium-dependent vascular relaxation are linked to chronic diabetes. The synthesis of nitric oxide (NO) is reduced in diabetic patients, resulting in vasodilation problems [11]. T2DM is thought to alter regional metabolism and

https://doi.org/10.46389/rjd-2022-1073

microcirculation by affecting glucose and insulin transport through the blood-brain barrier [12]. Chronic hyperglycemia has been shown to reduce regional blood flow and increase membrane permeability, resulting in long-term brain cell damage. Blood flow appears to be disrupted and white matter degeneration appears to be accelerated by a progressive metabolic disruption in the cerebrovascular bed [12].

Plasma visfatin has been linked to a variety of metabolic states in studies. Obesity, type 2 diabetes, metabolic syndrome, and cardiovascular disorders were all linked to an increase in it [6]. We discovered that diabetics with macro and micro-vascular complications had higher serum visfatin levels than diabetics without complications, but the difference was not statistically significant. Impaired glucose tolerance can cause omental adipose tissue to produce visfatin/Nampt to compensate for insulin resistance [13]. There was no substantial association between visfatin level and lab data such as creatinine, urea, or cholesterol level among the studied groups, according to our research. When comparing diabetic nephropathy cases to those without nephropathy, serum visfatin levels were significantly higher. Also, visfatin was found to be positively correlated with albumin/creatinine ratio [14], which contradicts our findings, as we found no association between visfatin and A/C ratio, but this may be due to sampling size differences, DM length in each category, and ethical differences.

Currently, over 20 cohort studies involving participants with and without prior vascular disease, as well as those with and without cardiovascular disease (CVD) risk factors, have consistently shown that higher cIMT values are linked to higher cardiovascular risk [15]. There was no major association between serum visfatin level and cIMT in diabetics with no macro-vascular complications and diabetics with macro-vascular complications, according to our findings. The large difference in DM period between the studied groups may explain this discrepancy in our sample. Among diabetics with macro-and microvascular complications, we discovered a strong positive association between cIMT and HbA_{1c} with a p-value (0.005, <0.001). Hyperglycemia causes oxidative stress, resulting in increased reactive oxygen species (ROS) formation and triggered cell injury, mediated primarily by four molecular pathways, and it's also associated with the development of free fatty acids (FFA) and growth factors, leading to cellular metabolism abnormality. Endothelial and mitochondrial damage will result as a result of this. Lipoprotein accumulation in the intimal surface is also caused by endothelial dysfunction. These LDS particles will clump together on a thickening intimal surface that is rich in proteoglycans, indicating the onset of atherosclerosis [16]. Patients with no complications and those with microvascular complications had a significant correlation between age and cIMT [17], and we found a significant correlation between age and cIMT with (p=0.004 and 0.013) patients with no complications and those with microvascular complications, respectively.

Our findings revealed that the pulsatility index of the right and left middle cerebral arteries (PI RT and LT MCA) has a substantial relationship with HBA_{1c} in diabetics with macro-vascular complications (p=0.001, 0.016) and microvascular complications (p=0.006, 0.002), respectively. The Gosling PI was designed to test vascular resistance, and this relationship was proven in normal human brachial arteries. As a result, the higher PI found in this study is likely due to increased cerebrovascular resistance in the cerebral circulation [18]. Aging has also been linked to a decrease in cerebral vessel flow velocity and an increase in pulsatility [18]. Our patients with microvascular and macrovascular problems were significantly older than those without, which may explain the differences in outcomes.

Increased pulsatility tends to be mostly due to microangiopathic damage to cerebral arterioles, given the presence of microangiopathy in other organs such as the retina, kidney, and peripheral nerve [18]. PI elevation determined by TCD has been linked to increased small vessel pathology such as white matter hyperintensities or lacunar infarctions in previous studies [19]. Patients with more severe white matter hyperintensities and chronic lacunar infarction had a higher MCA PI, according to the findings of our research. RT MCA PI and RT cIMT and LT cIMT

(p=0.013, 0.022) and LT MCA PI and RT cIMT and LT cIMT (p=0.001, 0.001) were found to have a positive significant association in diabetics with microvascular complications.

However, if cIMT thickening constitutes a general thickening of the inner layers of the arteries, including the smaller vessels, this could increase peripheral vascular resistance, increasing MCA PI, according to Poiseuille's rule. Large elastic arteries stiffening is linked to carotid plaque, cIMT, which MCA PI, and maybe a factor in the current study's findings [20].

The intracranial vascular disease has been diagnosed and predicted using TCD parameters [21]. It was also discovered that traditional cardiovascular risk factors such as age, sex, and diabetes had an impact on cerebral flow velocity [22]. We found that MCA PI can be used to predict microvascular complications with (p=0.002 and 0.001) and cut off value(1.005 and 1.035) for RT MCA PI, with sensitivity (69.2% and 64.1%) and specificity (75% and 95%) for RT MCA PI, respectively, which agreed with Lee, K. Y., et al. in part because their study defines TCD findings of diabetes-related cerebral hemodynamic changes and indicates that the PI represents micro-angiopathic changes in cerebral vessels [18]. While there was a lot of overlap in PI values between patient groups, only a few non-complicated patients had PI values of.0.8 for MCA, while a large percentage of complicated patients had PI values higher than these. These findings are insufficient to establish cutoff values for identifying complicated patients, but they do indicate that high PI values in these arteries above a certain threshold increase the risk of concomitant microvascular complications.

The hemisphere theory may explain the difference in ratio between the right and left MCA PI, as we discovered in our research. The left hemisphere of the brain is involved in auditory memory, especially for verbal content, while the right hemisphere is more involved in nonverbal memory. Aphasia is generally associated with problems in learning, hearing, and interpreting numbers in executive function. Aphasia is a condition that affects the non-dominant (left) hemisphere and is linked to damage in the MCA distribution region. It explains why subjects with an abnormal PI on the left side of the MCA have a higher risk of cognitive failure than those with an abnormal PI on the right side of the MCA [23].

Surprisingly, 7 out of 10 of our patients who underwent brain MRI with stroke protocol (MRI, MRA, MRI with diffusion) had bilateral lacunar infarctions, and 5 of those 7 had MCA PI greater than the cutoff value for both RT and LT MCA in both micro and macro-vascular groups. Patients with any small vessel disease (SVD) lesion (WMLsand/or lacunes) had significantly higher median values of MCA PI than those without SVD lesions, according to Sanahuja J., et al. [24].

According to the SONIA (stroke outcomes and neuroimaging of intracranial atherosclerosis) trial guidelines, the following MFV (mean flow velocity) cut-offs on TCD were used to identify a 50% stenosis: MFV>100 cm/second MCA [25]. Despite this, we found 15 patients with MCA MFV>100 cm/min, all of whom had MCA PI above the cut-off value, four of whom had MRI stroke protocol, three of whom revealed periventricular lacunar encephalopathy, and one of whom displayed RT MCA stenosis in the MRA with (RT MCA MFV=100 cm/min and PI=1.5), but none of whom had a clinical history of stroke or TIA. We may depend on the presence of good collaterals in this regard. Since collateral circulation is essential for maintaining the balance and efficiency of cerebral blood perfusion [26]. The collateral brain circulation system involves a secondary cerebral vessel network that connects the main cerebral arteries, and if a cerebral artery becomes blocked, the collateral vessels may help to restore normal cerebral blood flow [26].

In the current study, we discovered a positive significant association between serum visfatin level and PI basilar, RT, and LT MCA with (p=0.030, 0.001, =0.035) among diabetics with no complications, (p=0.001) in both macro and micro-vascular complications groups, and to our knowledge, no previous studies have established this correlation.

Conclusion

TCD is a non-invasive technique for determining brain circulation and predicting complications and prognosis in high-risk diabetics.

https://doi.org/10.46389/rjd-2022-1073

Acknowledgments

All authors have contributed significantly and equally in the design of this work, data acquisition, analysis, and interpretation. In addition to the writing and revising of this manuscript, all authors approved the final version before submission. The authors have declared that no conflict of interest exists. This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

Conflict of interest

The authors declare no conflict of interest.

References

1. Kadhum, N. J., Al-Mudheffer, Z. A., Hasson, H. K. (2016). Evaluation of cerebral vasoreactivity in type 2 diabetic patients by using transcranial doppler ultrasonography (TCD). *Thi-Qar Med J (TQMJ)*. 12(2):1–10.
2. Aljefree, N., Ahmed, F. (2015). Prevalence of cardiovascular disease and associated risk factors among adult population in the gulf region: a systematic review. *Adv Public Health*. 2015:1–23.
3. Meschia, J. F., Bushnell, C., Boden-Albala, B., et al. (2014). Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 45(12):3754–3832.
4. Adeghate, E. (2008). Visfatin: structure, function and relation to diabetes mellitus and other dysfunctions. *Curr Med Chem*. 15(18):1851–1862.
5. Toruner, F., Altinova, A. E., Bukan, N., et al. (2009). Plasma visfatin concentrations in subjects with type 1 diabetes mellitus. *Horm Res*. 72(1):33–37.
6. Di Raimo, T., Azzara, G., Corsi, M., Cipollone, D., Lo Vasco, V. R., Businaro, R. (2015). Adipokine and their involvement as a target of new drugs. *J Pharmacovig*. 3(3):166.
7. Lee, K. O., Lee, K. Y., Lee, S. Y., Ahn, C. W., Park, J. S. (2007). Lacunar infarction in type 2 diabetes is associated with an elevated intracranial arterial pulsatility index. *Yonsei Med J*. 48(5):802–806.
8. Chan, Y. H. (2003). Biostatistics 102: quantitative data--parametric & non-parametric tests. *Singapore Med J*. 44(8):391–396.
9. Chan, Y. H. (2003). Biostatistics 103: qualitative data - tests of independence. *Singapore Med J*. 44(10):498–503.
10. Chan, Y. H. (2003). Biostatistics 104: correlational analysis. *Singapore Med J*. 44(12):614–619.
11. Cipolla, M. J., Godfrey, J. A. (2010). Effect of hyperglycemia on brain penetrating arterioles and cerebral blood flow before and after ischemia/reperfusion. *Transl Stroke Res*. 1(2):127–134.
12. Jansen, J. F., van Bussel, F. C., van de Haar, H. J., et al. (2016). Cerebral blood flow, blood supply, and cognition in type 2 diabetes mellitus. *Sci Rep*. 6(1):10. Published 2016 Dec 5.
13. Goktas, Z., Owens, S., Boylan, M., et al. Associations between tissue visfatin/nicotinamide, phosphoribosyltransferase (Nampt), retinol binding protein-4, and vaspin concentrations and insulin resistance in morbidly obese subjects. *Mediators Inflamm*. 2013:861496.
14. Mageswari, R., Sridhar, M. G., Nandeesha, H., Parameshwaran, S., Vinod, K. V. (2019). Irisin and visfatin predicts severity of diabetic nephropathy. *Ind J Clin Biochem*. 34(3):342–346.
15. O'Leary, D. H., Bots, M. L. (2013). Imaging of atherosclerosis: carotid intima-media thickness. *Eur Heart J*. 31(14):1682–1689.
16. Pramayudha, R., Achmad, C., Erwinanto Martha, J. W., Akbar, M. R. (2019). Correlation between HbA1c levels with carotid intima media thickness in newly diagnosed type 2 diabetes mellitus patients. *ACI (Acta Cardiologia Indonesiana)*. 5(2):111–118.
17. Olt, S., Şirik, M., Baykan, A. H., Çeliker, M. (2016). The relationship between HbA1c and carotid intima-media thickness in type 2 diabetic patients. *The Pan Afr Med J*. 23:224.
18. Lee, K. Y., Sohn, Y. H., Baik, J. S., Kim, G. W., Kim, J. S. (2000). Arterial pulsatility as an index of cerebral microangiopathy in diabetes. *Stroke*. 31(5):1111–1115.
19. Yoon, Y., Lee, D. H., Kang, D. W., Kwon, S. U., Kim, J. S. (2013). Single subcortical infarction and atherosclerotic plaques in the middle cerebral artery: high-resolution magnetic resonance imaging findings. *Stroke*. 44(9):2462–2467.
20. Vigen, T., Ihle-Hansen, H., Lyngbakken, M. N., et al. Carotid atherosclerosis is associated with middle cerebral artery pulsatility index. *J Neuroimaging*. 30(2):233–239.
21. Han, M., Nam, H. S. (2018). Impact of asymmetric middle cerebral artery velocity on functional recovery in patients with transient ischemic attack or acute ischemic stroke. *Korean J Clin Lab Sci*. 50(2):126–135.
22. Wijnhoud, A. D., Koudstaal, P. J., Dippel, D. W. (2006). Relationships of transcranial blood flow Doppler parameters with major vascular risk factors: TCD study in patients with a recent TIA or nondisabling ischemic stroke. *J Clin Ultrasound*. 34(2):70–76.
23. Harris, S., Reyhan, T., Ramli, Y., Prihartono, J., Kurniawan, M. (2018). Middle cerebral artery pulsatility index as predictor of cognitive impairment in hypertensive patients. *Front Neurol*. 9:538.
24. Sanahuja, J., Alonso, N., Diez, J., et al. (2016). Increased burden of cerebral small vessel disease in patients with type 2 diabetes and retinopathy. *Diabetes Care*. 39(9):1614–1620.
25. Bathala, L., Mehndiratta, M. M., Sharma, V. K. (2013). Transcranial doppler: technique and common findings (Part 1). *Ann Indian Acad Neurol*. 16(2):174–179.
26. Chi, Y., Lu, Z. N. (2017). Association between patency of the circle of Willis and diabetes mellitus in patients with cerebral ischaemic stroke. *J Int Med Res*. 45(2):723–732.