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THE DIAGNOSTIC VALUE OF SERUM NEUROAPOPTOSIS-REGULATING INVERTASE (NARC1), VON WILLEBRAND FACTOR (vWF), AND PROTEIN G3A LEVELS IN TYPE 2 DIABETES PATIENTS WITH MACROVASCULAR LESIONS

DIJAGNOSTIČKA VREDNOST SERUMSKE INVERTAZE (NARC1) KOJA REGULIŠE NEUROAPOPTOZU, VON WILLEBRAND FAKTORA (vWF) I NIVOA PROTEINA G3A KOD PACIJENATA SA DIJABETESOM TIPA 2 I MAKROVASKULARNIM LEZIJAMA

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Summary

Background: To evaluate the diagnostic value of serum Neuroapoptosis-regulating invertase (NARC1), von Willebrand factor (vWF), and Protein G3a levels in type 2 diabetes patients complicated with macrovascular lesions.
Methods: The type 2 diabetes group consisted of 420 patients with the disease who were admitted to the hospital between January 2021 and June 2024. One hundred fifty healthy people who visited this hospital for checkups during the same time frame were selected for the healthy control group. Based on the diagnostic criteria for macrovascular disease, individuals with type 2 diabetes were split into two groups: 236 patients with uncomplicated diabetes and 184 patients with macrovascular disease. Changes in serum NARC1, vWF, and Protein G3a levels were observed in each group. Serum NARC1, vWF, and Protein G3a levels in individuals with type 2 diabetes were compared before and after treatment using univariate analysis, and the diagnostic efficacy of these three indicators for macrovascular disease in patients with type 2 diabetes was assessed.
Results: Serum NARC1 and vWF levels were significantly greater in the type 2 diabetes group, although serum Protein G3a levels were significantly lower ($P<0.05$) than in the healthy control group. Before therapy, the macrovascular lesion group's serum NARC1 and vWF levels were consider-

Kratak sadržaj

Uvod: Procena dijagnostičke vrednosti serumske invertaze koja reguliše neuroapoptozu (NARC1), von Willebrand faktora (vWF) i nivoa proteina G3a kod pacijenata sa dijabetesom tipa 2 komplikovanim makrovaskularnim lezijama.
Metode: Grupu sa dijabetesom tipa 2 činilo je 420 pacijenata hospitalizovanih u periodu od januara 2021. do juna 2024. godine. Kao kontrolna grupa izabrano je 150 zdravih osoba koje su se u istom periodu javile na rutinske preglede. Prema dijagnostičkim kriterijumima za makrovaskularne bolesti, pacijenti sa dijabetesom tipa 2 podeljeni su na dve podgrupe: 236 pacijenata sa nekomplikovanim dijabetesom i 184 pacijenta sa makrovaskularnim oboljenjem. U obe grupe praćene su promene nivoa serumskog NARC1, vWF i proteina G3a. Upotrebom univarijante analize upoređivani su nivoi serumskog NARC1, vWF i proteina G3a kod pacijenata sa dijabetesom tipa 2 pre i nakon terapije, a takođe je ispitana dijagnostička efikasnost ova tri biomarkera za makrovaskularne lezije udružene sa dijabetesom tipa 2.
Rezultati: Nivoi serumskog NARC1 i vWF su bili značajno viši u grupi sa dijabetesom tipa 2, dok su nivoi proteina G3a bili značajno niži ($P<0,05$) u poređenju sa zdravom kontrolnom grupom. Pre terapije, grupa sa makrovaskularnim lezijama imala je značajno više nivoe serumskog

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ably higher than those of the simple diabetes group (P<0.05). After treatment, the levels of serum NARC1 and vWF in both groups were significantly lower than those before treatment. However, levels in the macrovascular lesion group remained higher than those in the simple diabetes group, and the difference was statistically significant (P<0.05). Before therapy, the macrovascular lesion group's serum Protein G3a level was significantly lower than that of the simple diabetes group (P<0.05). Although the difference was statistically significant (P<0.05), the group with macrovascular lesions still had a lower level than the group with simple diabetes. According to univariate analysis, the proportions of people aged ≥60 and with a diabetes course of ≥10 years, as well as low-density lipoprotein cholesterol and triglyceride levels, were considerably greater in the group with macrovascular lesions than in the group with uncomplicated diabetes, and the differences were statistically significant (P<0.05). Multivariate analysis revealed that patients with type 2 diabetes mellitus, increased levels of NARC1 and vWF were independent risk factors for macrovascular disease (P<0.05), whereas elevated serum Protein G3a levels were a protective factor for macrovascular disease in type 2 diabetes mellitus patients (P<0.05). The sensitivity of the combined detection of serum NARC1, vWF, and Protein G3a in diagnosing type 2 diabetes complicated with macrovascular lesions was 89.4%, the specificity was 90.0%, and the area under the curve (AUC) was 0.959. The AUC was significantly greater than that of NARC1 (Z=4.160, P<0.01) and vWF (Z=4.059, P<0.01). However, individual Protein G3a indications were found (Z=5.186, P<0.01).
Conclusions: NARC1, vWF, and Protein G3a are involved in macrovascular disease in patients with type 2 diabetes. When these three indicators are detected together, they are highly effective at identifying macrovascular disease complicated by type 2 diabetes.

Keywords: type 2 diabetes, macrovascular disease, neuroapoptosis-regulating invertase, von Willebrand factor, Protein G3a

NARC1 i vWF u odnosu na grupu sa nekomplikovanim dijabetesom (P<0,05). Nakon terapije, u obe grupe je zabeleženo značajno smanjenje nivoa NARC1 i vWF, ali su vrednosti u grupi sa makrovaskularnim lezijama ostale više nego u grupi sa prostim dijabetesom (P<0,05). Pre terapije, nivoi proteina G3a u grupi sa makrovaskularnim lezijama bili su značajno niži nego u grupi sa nekomplikovanim dijabetesom (P<0,05) i ostali su niži i nakon terapije (P<0,05). Prema univarijantnoj analizi, veći udeo osoba starijih od 60 godina, dužina trajanja dijabetesa ≥10 godina, kao i viši nivoi LDL-holesterola i triglicerida zabeleženi su u grupi sa makrovaskularnim lezijama, u poređenju sa grupom sa nekomplikovanim dijabetesom (P<0,05). Multivarijantna analiza je pokazala da su povišeni nivoi NARC1 i vWF nezavisni faktori rizika za makrovaskularnu bolest u dijabetesu tipa 2 (P<0,05), dok je povišen nivo proteina G3a bio zaštitni faktor (P<0,05). Kombinovana detekcija NARC1, vWF i proteina G3a pokazala je senzitivnost od 89,4%, specifičnost od 90,0% i površinu ispod krive (AUC) od 0,959, što je bilo značajno više u odnosu na pojedinačne pokazatelje NARC1 (Z=4,160, P<0,01) i vWF (Z=4,059, P<0,01), kao i proteina G3a (Z=5,186, P<0,01).
Zaključak: NARC1, vWF i protein G3a učestvuju u razvoju makrovaskularnih bolesti kod pacijenata sa dijabetesom tipa 2. Njihova kombinovana detekcija pokazuje visoku dijagnostičku vrednost u identifikaciji makrovaskularnih lezija udruženih sa dijabetesom tipa 2.

Ključne reči: dijabetes tipa 2, makrovaskularna bolest, invertaza koja reguliše neuroapoptozu (NARC1), von Willebrand faktor (vWF), protein G3a

Introduction

Type 2 diabetes is becoming more common each year and is a significant health risk to people. Disorders of glucose metabolism are the primary feature of type 2 diabetes, which frequently affects the heart, kidneys, limbs, and other organs (1–3). More than 70% of patients will develop macrovascular lesions. Therefore, early detection of high-risk groups for macrovascular lesions and timely adoption of corresponding intervention measures are the keys to reducing the incidence of complications and improving quality of life. At present, the specific pathogenesis of macrovascular lesions remains unclear, and they are mainly related to atherosclerosis of the vascular arteries to some extent (4). At present, the diagnosis of macrovascular lesions relies mainly on arteriography, but it is expensive, and the misdiagnosis rate remains relatively high. In recent years, blood markers have been increasingly applied in clinical practice and play an important role in the diagnosis of macrovascular lesions (5). Neuroapoptosis-regulating invertase (NARC1), synthesized by the liver, is a serine kinase that aggravates lipid metabolism disorders and vascular endothelial damage by reducing the breakdown of low-density lipoprotein (6–8). Von Willebrand factor (vWF) is a cytokine secreted by damaged vascular endothelial cells and is an important marker of endothelial cell dysfunction and damage. The Protein G3a promotes inflammation and is involved in the lipid metabolism process (9). Its chronic complications, especially macrovascular lesions involving the heart, brain, lower extremities, etc., are the main causes of disability and death among patients, constituting a heavy public health burden (10). Type 2 diabetes mellitus (T2DM) patients' clinical evaluation of macrovascular risk currently relies primarily on imaging tests and conventional risk factors (such as blood pressure, lipid profiles, and glycemic control). However, there is still a lack of highly sensitive and specific early warning and diagnostic biomarkers, leading to the failure to timely identify and intervene for some high-risk patients (11). Serum preprotein convertase subtilisin 9 (NARC1) not only regulates the metabolism of low-density lipoprotein cholesterol

but also has proinflammatory and proatherosclerotic effects (12–14). Von Willebrand factor (vWF), a key marker of endothelial injury and dysfunction, is involved in thrombosis and vascular lesions. Protein G3a is an important component of high-density lipoprotein and exerts anti-inflammatory, antioxidant, and vasoprotective effects by influencing cholesterol reverse transport and the sphingosinol-1-phosphate signaling pathway (15). These three factors play important roles in the core pathophysiological mechanisms underlying large vessel lesions in T2DM, including disorders of glycolipid metabolism, endothelial injury, inflammatory activation, and atherosclerosis (16–18). However, little research has been done on the effectiveness of measuring blood NARC1, vWF, and Protein G3a levels in tandem to identify macrovascular lesions in people with type 2 diabetes.

Our study intends to investigate the evolving features of serum levels of Protein G3a, vWF, and NARC1 in individuals with type 2 diabetes who also have macrovascular disease, evaluate the potential diagnostic value of their individual and combined application for this complication, and provide new laboratory evidence for the early identification of high-risk populations and the formulation of intervention strategies.

Materials and Methods

General information

A total of 420 patients with type 2 diabetes, 248 males and 172 females, who visited our hospital between January 2021 and June 2024, were included in the type 2 diabetes group. The age ranged from 45 to 79 years, with an average of 63.21±7.85 years, and the body mass index (BMI) was 23.87±1.57 kg/m^2.

The inclusion criterion was that all patients met the diagnostic criteria for type 2 diabetes. All patients were treated with oral hypoglycemic drugs and exercise therapy, and none of them had received insulin treatment. The exclusion criteria for patients were type 1 diabetes and severe functional disorders of organs such as the heart, liver, and kidneys. Acute and chronic infectious diseases are combined with ketoacidosis or other severe diabetic complications; pregnant and lactating women are combined with malignant tumors and hematological or immune diseases.

Type 2 diabetes is diagnosed when a person meets any one of the following criteria and exhibits typical diabetes symptoms: Blood glucose levels of 7.0 mmol/L for fasting plasma glucose (FPG), 11.1 mmol/L for 2-hour postprandial blood glucose (2hPG), or 11.1 mmol/L for blood glucose at any time. If a patient meets any one of the following criteria, they can be diagnosed with combined macrovascular disease: having a history of cerebrovascular accident or having ischemic foci found during head CT or MRI examination; having a history of angina pectoris and myocardial infarction or having been diagnosed with coronary heart disease by coronary angiography; and color Doppler ultrasound examination showing that the carotid intima media thickness (IMT) is ≥1.0 mm. Color Doppler ultrasound examination revealed extensive and irregular stenosis of the lower extremity blood vessels (with segmental occlusion or vessel diameter <3 mm).

The healthy control group consisted of 150 healthy individuals who underwent examinations at our hospital during the same time period; 82 were men, and 64 were women. The age ranged from 45 to 79 years, with an average of 62.96±8.21 years. The BMI was 23.11±1.66 kg/m^2. The baseline statistics for the two groups of research volunteers were equivalent and did not differ significantly in age, sex, or BMI ($P>0.05$). Every participant in the study signed the informed consent form. The medical ethics committee at our hospital approved this study [No. HKYS-2025-A0240].

Treatment methods

After admission, patients with type 2 diabetes were given exercise therapy, dietary control, and drug treatment. They were given 0.5 g of sustained-release metformin tablets twice a day, with or after meals. Sitagliptin phosphate (100 mg) was administered once daily. The medication was adjusted based on blood sugar levels to keep it within the target range. All diabetic patients received continuous treatment and were evaluated after 6 months.

Laboratory index detection

At admission and 6 months after treatment, 6 mL of fasting elbow venous blood samples were collected from healthy controls. To identify serum NARC1, vWF, and Protein G3a levels, three milliliters of the sample were put in an anticoagulant tube and centrifuged for ten minutes at 3,000 rpm. Repeated freezing and thawing cycles were avoided. Another 3 mL of each blood sample was used to detect biochemical indicators: FPG and 2hPG were measured by the glucose oxidase method, and HbA1c was determined with a glycated hemoglobin (HbA1c) meter. Triglycerides (TGs), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were measured using an automatic biochemical analyzer.

Detection of the IMT in the neck

The carotid arteries of patients were detected using color Doppler ultrasound (model PHLIP-7500),

with the ultrasound probe frequency ranging from 7.5 to 10.0 MHz. For the specific operation, a pillow was placed at the back of the neck, the head was tilted back, and the head was turned to one side to expose the neck fully. A probe was used to explore the bilateral common carotid arteries. The distal bifurcation of the common carotid arteries was used to measure the vertical distance between the intimal and medial surfaces.

Observation indicators

Changes in the serum NARC1, vWF and Protein G3a levels in the two groups were observed, the influencing factors of type 2 diabetes complicated with macrovascular disease were analyzed, the changes in the serum NARC1, vWF and Protein G3a levels in patients with type 2 diabetes before and after treatment were evaluated, and their diagnostic efficacy in type 2 diabetes complicated with macrovascular disease was assessed.

Statistical processing methods

The data was handled, and statistical analysis was carried out using SPSS 22.0. The measurement data follow a normal distribution and are shown as x ± s. Independent-samples t tests were used to compare data between two groups, whereas paired-samples t tests were used to compare data before and after treatment. The χ^2 test was used for group comparisons, and count statistics are presented as percentages or as counts. Receiver operating characteristic (ROC) curves were used to assess the diagnostic utility of blood NARC1, vWF, and Protein G3a levels in patients with type 2 diabetes who had complex macrovascular lesions.

Results

Comparison of serum NARC1, vWF, and Protein G3a levels between the two groups

The type 2 diabetes group's serum NARC1 and vWF levels were significantly greater than those of the healthy control group, although their serum Protein G3a levels were significantly lower ($P<0.05$), see *Table I*.

Serum NARC1, vWF, and Protein G3a levels in type 2 diabetic patients before and after therapy

There were two groups of individuals with type 2 diabetes: 236 patients with uncomplicated diabetes and 184 patients with macrovascular disease according to the diagnostic criteria for macrovascular disease. Serum NARC1 and vWF levels were substantially greater in the group with macrovascular lesions than in the group with uncomplicated diabetes before

Table I Comparison of serum NARC1, vWF, and Protein G3a levels between the two groups.

Group	n	NARC1 (ng/mL)	vWF (μmol/L)	Protein G3a (μg/mL)
Healthy control group	150	85.40±23.85	8.14±2.11	12.46±2.11
Type 2 diabetes group	420	110.31±27.84	20.77±6.64	8.55±2.14
t	–	6.907	24.246	13.659
P	–	<0.001	<0.001	<0.001

Table II Changes of serum NARC1, vWF, and Protein G3a levels in patients with type 2 diabetes before and after treatment.

Group	n	NARC1 (ng/mL)		vWF (μmol/L)		Protein G3a (μg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Large vessel disease group	184	129.71±26.12	98.76±17.22	24.38±6.69	18.45±4.21	7.24±1.79	9.16±2.11
Simple diabetes group	236	95.28±17.97	90.85±15.85	17.95±5.06	14.31±3.87	9.57±1.70	11.85±2.85
t		10.826	3.454	7.703	7.196	9.476	7.559
P		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table III Single-factor analysis of type 2 diabetes complicated with macroangiopathy.

Group	n	Gender		Age (years)		Course of diabetes (years)		BMI (kg/m^2)	
		Male	Female	≥60	≤60	≥10	<10	≥23	<23
Simple diabetes group	236	134	102	122	114	106	130	136	100
Large vessel disease group	184	114	70	126	58	112	72	112	72
x^2/t		0.372		5.341		4.654		0.114	
P		0.531		0.024		0.034		0.732	
Group	n	FPG (mmol/L)		2 h PG (mmol/L)		HbAlc (%)	SBP (mm Hg)	DBP (mmHg)	
Simple diabetes group	236	8.47±2.35		10.60±2.20		8.98±0.87	133.47±15.14	75.61±10.30	
Large vessel disease group	184	8.77±1.43		10.97±2.48		9.13±1.02	137.79±16.69	74.79±9.74	
x^2/t		1.169		0.806		1.072	1.968	0.656	
P		0.275		0.426		0.285	0.054	0.517	
Group	n	TG (mmol/L)		TC (mmol/L)		LDL-C (mmol/L)		HDL-C (mmol/L)	
Simple diabetes group	236	2.88±0.86		4.39±1.15		3.44±0.81		1.19±0.34	
Large vessel disease group	184	3.15±1.08		4.56±0.92		3.95±0.96		1.11±0.36	
x^2/t		2.106		1.185		4.045		0.231	
P		0.030		0.231		<0.001		0.751	

therapy (P<0.05). Both groups' serum NARC1 and vWF levels were significantly lower after treatment than they were before. Still, the macrovascular lesion group's levels were higher than the simple diabetes group's, and the difference was statistically significant (P<0.05). The group with macrovascular lesions had a significantly lower blood Protein G3a level before therapy than the group with uncomplicated diabetes (P<0.05). Serum Protein G3a levels in both groups were considerably higher following treatment than they were before it. However, the group with macrovascular lesions and the group with uncomplicated diabetes differed statistically significantly (P<0.05), see *Table II*.

Univariate analysis of macrovascular lesions in type 2 diabetes mellitus patients

The proportions of patients aged ≥60 years and those with a diabetes duration of ≥10 years, as well as the levels of TG and LDL-C in the macrovascular lesion group, were significantly greater than those in the simple diabetes group (P<0.05). There was no statistically significant difference between the two groups in sex, BMI≥23 kg/m^2, FPG, 2hPG, HbA1c, systolic and diastolic blood pressure (SBP and DBP), TC, or HDL-C (P>0.05), see *Table III*.

Multivariate analysis of macrovascular lesions in type 2 diabetes mellitus patients

Age, duration of diabetes, TG, LDL-C, NARC1, vWF, and Protein G3a showed statistically significant differences between groups with uncomplicated diabetes and those with macrovascular lesions. Multivariate logistic regression analysis was then conducted utilizing these indicators. While elevated serum Protein G3a levels were a protective factor against macrovascular disease, elevated levels of NARC1 and vWF were independent risk factors for macrovascular disease (see *Table IV*).

Table IV Multifactor analysis of type 2 diabetes complicated with macroangiopathy.

Indicator	β	Standard deviation	Wald x^2	P	OR	95% CI
Age	-1.535	1.358	1.272	0.251	0.219	0.018~3.079
Course of diabetes	2.288	1.336	2.943	0.089	9.822	0.724~133.947
TG	0.503	0.348	2.090	0.141	1.642	0.831~3.248
LDL-C	0.562	0.357	2.594	0.100	1.760	0.886~3.538
NARC1	0.093	0.012	22.861	<0.001	1.097	1.057~1.138
vWF	0.197	0.055	13.669	<0.001	1.217	1.098~1.348
Protein G3a	-0.914	0.214	18.609	<0.001	0.405	0.269~0.601

Table V Diagnostic efficacy of serum NARC1, vWF, and Protein G3a levels in macrovascular complications of type 2 diabetes.

Indicator	Truncation value	Sensitivity (%)	Specificity (%)	AUC	95% CI
NARC1	112.74 ng/mL	72.1	86.7	0.850	0.806~0.905
vWF	22.32 μmol/L	71.0	82.5	0.824	0.765~0.873
Protein G3a	8.03 μg/mL	70.0	83.4	0.821	0.773~0.879
NARC1+WF+ Protein G3a	–	89.4	90.0	0.959	0.912~0.983

Diagnostic efficacy of serum NARC1, vWF, and Protein G3a levels in type 2 diabetes complicated with macrovascular lesions

The levels of serum NARC1, vWF, and Protein G3a have high diagnostic efficacy in type 2 diabetes complicated with macrovascular lesions. To determine if macrovascular lesions developed in patients with type 2 diabetes, multivariate logistic regression analysis was conducted on the levels of serum NARC1, vWF, and Protein G3a, and the equation Y=0.08X NARC1+0.24X vWF-0.96X Protein G3a-6.33 was used as the combined detection index. The sensitivity of the combined detection method was 89.1%, the specificity was 90.0%, and the AUC was 0.959. Its AUC was significantly greater than that of the individual indicators NARC1 (Z=4.160, P<0.01), vWF (Z=4.059, P<0.01), and Protein G3a (Z= 5.186, P<0.01), whereas the AUC among the three indicators was not significantly different in the C comparison (P>0.05), see *Table V.*

Discussion

The most significant complication of diabetes is macrovascular disease, which mainly includes peripheral vascular disease and cerebrovascular disease (19). The main pathological and physiological change leading to macrovascular lesions is atherosclerosis. The inflammatory response triggered by disorders of glucose metabolism is a major driver of atherosclerosis. The level of NARC1 fluctuates significantly in the body, showing a notable increase after meals and a significant decrease after fasting (20–22). Moreover, changes in its level are diurnal and are associated with cholesterol synthesis. Both the group with simple diabetes and the group with macrovascular disease experienced a significant drop in serum NARC1 levels following treatment (23). Nevertheless, following therapy, the macrovascular lesion group's blood NARC1 level remained higher than that of the simple diabetes group, suggesting a close relationship between NARC1 levels and type 2 diabetes and the development of macrovascular lesions. Basic research has confirmed that NARC1 can reduce the expression of LDL-C receptors on the surface of liver cells, thereby reducing LDL-C uptake by the body and, subsequently, increasing serum LDL-C levels. Another study confirmed that the level of NARC1 in patients with pancreatic β-cell tumors is significantly elevated. It can activate glucokinase by inhibiting NARC1 expression, thereby reducing blood sugar levels. Single-factor analysis revealed that the proportions of individuals aged ≥60 years and diabetes duration ≥10 years, as well as the levels of TG and LDL-C in the macrovascular lesion group, were significantly greater than those

in the simple diabetes group ($P<0.05$), whereas comparisons of sex, BMI≥23 kg/m^2, and FPG, 2hPG, HbA1c, SBP, DBP, TC, and HDL-C values did not show any statistically significant variations (24). When the serum NARC1 level was 112.74 ng/mL, the sensitivity for diagnosing macrovascular lesions was 72.1%, the specificity was 86.7%, and the AUC was 0.850, demonstrating high diagnostic efficacy and providing a reference for whether further intervention is needed for these patients.

vWF mainly enhances platelet activity and promotes the formation of microthrombi and the subcutaneous adhesion and aggregation of platelets within blood vessels, thereby leading to thrombosis and the development of macrovascular diseases (25). When vascular endothelial cells are damaged, a large amount of vWF is released from Weibel-Palade bodies. Moreover, exposure of the vascular basement membrane triggers the endogenous coagulation cascade, leading to the synthesis and release of vWF by endothelial cells. Moreover, vWF can bind to platelet membrane receptors, causing platelets to adhere to endothelial cells, activating platelets and promoting thrombosis formation (26). Moreover, vWF is closely related to the development of type 2 diabetes and macrovascular disease. This finding is consistent with the conclusion of a previous study (27) that vWF levels in patients with type 2 diabetes complicated by macrovascular disease are significantly higher than those in patients without macrovascular disease. During the long course of diabetes, multiple factors lead to damage to vascular endothelial cells, promoting an increase in the body's vWF levels, providing conditions for platelet adhesion, and facilitating the formation of vascular lesions. When the serum vWF level in diabetic patients is 22.32 μmol/L, the sensitivity for diagnosing macrovascular disease is 71.0%, the specificity is 82.5%, and the AUC is 0.824, indicating that the serum vWF level has high diagnostic efficacy for predicting macrovascular disease in patients with type 2 diabetes (28–30).

Protein G3a is a protein capable of binding to lipids, which can activate various lipoprotein metabolic enzymes and regulate lipoprotein metabolism. Moreover, it can bind to lipoprotein receptors and participate in the regulation of lipid metabolism. Basic research shows that Protein G3a is a vital prerequisite substance for the synthesis of HDL-C and has a regulatory effect on the synthesis of HDL-C, thereby affecting lipid metabolism (31). After treatment, the serum Protein G3a level in both groups increased, indicating that Protein G3a is involved in lipid metabolism and vascular lesion formation in diabetes (32). The group with macrovascular disease had a substantially lower blood Protein G3a level than the group with uncomplicated diabetes (33). Serum Protein G3a levels in both groups were considerably higher following therapy than they were before it. In the macrovascular disease group, the serum Protein G3a level remained lower than in the uncomplicated diabetes group, indicating that Protein G3a has a significant regulatory effect on lipid metabolism and atherosclerosis (34–36). Its sensitivity is 89.1%, and its specificity is 90.7%, indicating that the three indicators have complementary roles in predicting macrovascular lesions and can improve diagnostic efficacy. The specific mechanism needs further study.

Conclusion

NARC1, vWF, and Protein G3a are involved in macrovascular disease in patients with type 2 diabetes. The diagnosis of macrovascular disease complicated by type 2 diabetes can be made with high diagnostic efficiency when all three signs are present.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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