



## Correlation of the carotid intima-media unevenness and stiffness with serum illness indexes in patients with type 2 diabetes mellitus

Ming-Rong Yang<sup>1</sup>✉, Zhi-Hua Shao<sup>2</sup>

<sup>1</sup> Department of Ultrasonography, 57 Branch of Hubei Qianjiang Jiangnan Oilfield General Hospital, Qianjiang 433121, China

<sup>2</sup> Department of Function, the Third Affiliated Hospital of Baotou Medical College in Inner Mongolia, Baotou 014010, China

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### ABSTRACT

**Objective:** To investigate the correlation of the carotid intima-media unevenness and stiffness with serum illness indexes in patients with type 2 diabetes mellitus. **Methods:** A total of 118 patients with type 2 diabetes mellitus who were treated in this hospital between February 2016 and August 2017 were selected as the diabetes group, and 100 healthy volunteers who received physical examination in this hospital during the same period were selected as normal control group. The differences in carotid intima-media unevenness and stiffness levels as well as serum levels of insulin resistance indexes and inflammatory adipocytokines were compared between the two groups of subjects. Pearson test was used to assess the correlation between carotid intima-media parameter levels and above serum illness index levels in patients with type 2 diabetes mellitus. **Results:** IMIsqrt and PWV levels in diabetes group were higher than those in normal control group; serum FINS and IRI levels were higher than those in normal control group whereas ISI level was lower than that in normal control group; serum APN content was lower than that in normal control group whereas LEP and SAA contents were higher than those in normal control group. Pearson test showed that the IMIsqrt and PWV levels in patients with type 2 diabetes mellitus were directly correlated with serum insulin resistance index levels and inflammatory adipocytokine contents. **Conclusion:** Carotid intima-media unevenness and stiffness both increase in patients with type 2 diabetes mellitus, and could objectively reflect the insulin resistance and systemic micro-inflammatory state.

## 1. Introduction

Carotid intima-media parameters are the common indicators to clinically evaluate the degree of atherosclerosis and the risk of cerebrovascular diseases, and current studies have shown that there are carotid intima-media lesions in a large proportion of patients with type 2 diabetes[1,2]. Both unevenness and stiffness are the most common carotid intima-media parameters, their levels gradually increase with the arterial lipid deposition and atherosclerosis formation[3,4], and there is still no final conclusion whether the carotid lesions in patients with type 2 diabetes are in accordance with the specific endocrine disorder, in other words, whether the carotid ultrasonography can be the simple and noninvasive

method to judge the condition of diabetes. In this study, the carotid unevenness and stiffness levels in patients with newly diagnosed type 2 diabetes mellitus were detected, and the inner link of their specific levels with serum insulin resistance and micro-inflammatory state was discussed in order to clarify the significance of carotid lesions for diabetes condition assessment.

## 2. Information and methods

### 2.1 Case information

A total of 118 patients with type 2 diabetes mellitus who were treated in this hospital between February 2016 and August 2017 were enrolled in diabetes group, and 100 healthy volunteers who received physical examination in this hospital during the same period were enrolled in normal control group. There were 62 male

✉ Corresponding author: Ming-Rong Yang, Department of Ultrasonography, 57 Branch of Hubei Qianjiang Jiangnan Oilfield General Hospital, Qianjiang 433121, China.

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cases and 56 female cases in the diabetes group, and they were 43-79 years old; normal control group included 51 male cases and 49 female cases that were 40-77 years old. The baseline data were comparable between the two groups, the patients themselves signed informed consent, and the hospital ethics committee approved the study plan.

### 2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with type 2 diabetes mellitus for the first time and receiving no systematic treatment outside the hospital; (2) cooperating with the related inspection, and no midway dropping out. Exclusion criteria: (1) combined with hyperthyroidism, hypothyroidism and other endocrine diseases; (2) combined with clear infectious diseases of tissue organs; (3) combined with severe heart, liver and kidney insufficiency.

### 2.3 Carotid intima-media parameters

Immediately after admission, color Doppler diasonograph was used for carotid ultrasonography of both groups, and the intima-media parameters, such as the square root of unevenness (IMIsqrt) and pulse wave velocity (PWV) were obtained.

### 2.4 Serum illness indexes

Immediately after admission, the fasting peripheral blood serum samples of the two groups of subjects were obtained and stored in a cryogenic environment. The glucometer was used to measure fasting insulin (FINS) level, and the insulin sensitivity index (ISI) and insulin resistance index (IRI) were calculated. The enzyme-linked immunosorbent assay was used to determine the serum contents of inflammatory adipocytokines (APN), leptin (LEP) and serum amyloid A (SAA) in.

### 2.5 Statistical methods

Carotid intima-media parameters, insulin resistance and inflammatory adipocytokines are all in terms of mean  $\pm$  standard deviation and compared by *t* test. The above data were input and calculated in SPSS 25.0 software, and obtained  $P < 0.05$  was the standard of statistical significance in differences between two groups.

## 3. Results

### 3.1 Carotid intima-media parameters

Comparison of carotid intima-media IMIsqrt and PWV levels between two groups of research subjects was as follows: IMIsqrt (0.71 $\pm$ 0.09) and PWV (8.74 $\pm$ 0.91) m/s in diabetes group were

higher than IMIsqr (0.48 $\pm$ 0.06) and PWV (7.16 $\pm$ 0.83) m/s in normal control group. Differences in carotid intima-media IMIsqrt and PWV levels were statistically significant between two groups of research subjects ( $P < 0.05$ ), shown in Table 1.

**Table 1.**

Comparison of carotid intima-media parameter levels between two groups of research subjects.

Groups	<i>n</i>	IMIsqrt	PWV
Control group	100	0.48 $\pm$ 0.06	7.16 $\pm$ 0.83
Diabetes group	118	0.71 $\pm$ 0.09	8.74 $\pm$ 0.91
<i>t</i>		6.392	5.935
<i>P</i>		<0.05	<0.05

### 3.2 Insulin resistance

Comparison of serum insulin resistance indexes FINS (IU/mL), ISI and IRI levels between two groups of research subjects was as follows: serum FINS and IRI levels in diabetes group were higher than those in normal control group whereas ISI level was lower than that in normal control group. Differences in serum insulin resistance indexes FINS, ISI and IRI levels were statistically significant between two groups of research subjects ( $P < 0.05$ ), shown in Table 2.

**Table 2.**

Comparison of insulin resistance degree between two groups of research subjects.

Groups	<i>n</i>	FINS	ISI	IRI
Control group	100	38.29 $\pm$ 4.51	0.72 $\pm$ 0.09	2.76 $\pm$ 0.29
Diabetes group	118	57.61 $\pm$ 6.09	0.41 $\pm$ 0.05	6.11 $\pm$ 0.74
<i>t</i>		14.921	7.024	9.282
<i>P</i>		<0.05	<0.05	<0.05

### 3.3 Inflammatory adipocytokines

Comparison of serum inflammatory adipocytokines APN (mg/L), LEP (ng/mL) and SAA ( $\mu$ g/L) contents between two groups of research subjects was as follows: serum APN content in diabetes group was lower than that in normal control group whereas LEP and SAA contents were higher than those in normal control group. Differences in serum inflammatory adipocytokines APN, LEP and SAA contents were statistically significant between two groups of research subjects ( $P < 0.05$ ), shown in Table 3.

**Table 3.**

Comparison of serum inflammatory adipocytokine contents between two groups of research subjects.

Groups	<i>n</i>	APN	LEP	SAA
Control group	100	8.93 $\pm$ 0.97	114.38 $\pm$ 13.59	42.82 $\pm$ 5.98
Diabetes group	118	6.56 $\pm$ 0.72	158.62 $\pm$ 17.29	76.14 $\pm$ 8.63
<i>t</i>		7.316	14.294	15.392
<i>P</i>		<0.05	<0.05	<0.05

### 3.4 Correlation analysis

Analysis of the correlation between carotid intima-media parameters and serum illness indexes in type 2 diabetes mellitus was as follows: the carotid intima-media IMIsqrt and PWV levels in patients with type 2 diabetes mellitus were positively correlated with insulin resistance indexes FINS and IRI levels and negatively correlated with ISI level; they were negatively correlated with inflammatory adipocytokine APN content and positively correlated with LEP and SAA contents ( $P < 0.05$ ), shown in Table 4.

**Table 4.**

The correlation between carotid intima-media parameters and serum illness indexes in type 2 diabetes mellitus.

Indexes	IMIsqrt		PWV	
	Determination coefficient r	P	Determination coefficient r	P
FINS	0.711	0.000	0.694	0.000
ISI	-0.684	0.007	-0.705	0.000
IRI	0.596	0.021	0.588	0.027
APN	-0.627	0.015	-0.611	0.017
LEP	0.598	0.019	0.574	0.031
SAA	0.732	0.000	0.702	0.000

## 4. Discussion

Type 2 diabetes mellitus is the most common clinical endocrine disorder, long-term abnormal glucose metabolism can damage blood vessels and cause a series of complications, and the carotid injury and atheromatous plaque formation are the relatively common and serious types. There are already carotid plaques in patients with initial type 2 diabetes mellitus, they are caused after the blood glucose fluctuations damage vascular endothelial cells, induce mononuclear macrophages and neutrophils to gather and activate platelet activity, some scholars have put forward that there is close relationship between carotid lesion degree and overall illness in diabetic patients, but no in-depth study confirms the speculation. Unevenness and stiffness are the common indicators to evaluate the artery function, there will be lipid and load sugar accumulation at the beginning of the formation of atherosclerosis, fibrous tissue hyperplasia results in the gradually stretching of intima-media, and it may induce the carotid artery occlusion when it cannot bear the fiber and calcium deposition[5–7]. During the above pathological changes, fibrous tissue deposits in different parts of the carotid artery and forms unevenness, and the more severe the carotid artery disease, the higher the unevenness[8,9]. The formation of stiffness is similar to that of unevenness. When the lipid deposits in the carotid artery, the stiffness increases and is manifested as the increase of PWV level in the specific numerical value[10]. The study showed that the carotid artery IMIsqrt and PWV levels in the diabetes group were higher than those in the normal control group, which confirms the presence of carotid artery disease in type 2 diabetic patients. The correlation of carotid IMIsqrt and PWV levels with diabetes mellitus

is discussed in the following parts.

Insulin resistance is the root cause of type 2 diabetes mellitus and also contributes to the progression of the disease. When the body's sensitivity to insulin is not enough, more insulin is secreted as feedback in order to maintain stable blood sugar and it forms hyperinsulinemia. With the islet  $\beta$  cell function damage and insulin resistance increase, the blood sugar fluctuates and a series of clinical responses are formed[11–13]. At present, the core role of clinical drugs is to improve insulin resistance and increase insulin sensitivity, so insulin resistance can directly reflect the condition of diabetes[14,15]. The study showed that FINS and IRI levels in diabetes group were higher than those in normal control group whereas ISI level was lower than that in normal control group, which is consistent with the condition of type 2 diabetes mellitus. Further Pearson test showed that IMIsqrt and PWV levels in patients with type 2 diabetes mellitus were positively correlated with FINS and IRI levels and negatively correlated with ISI level, confirming that the ultrasonic carotid intima-media unevenness and stiffness in patients with type 2 diabetes mellitus are positively correlated with the insulin resistance extent, in other words, the ultrasonic carotid artery lesion severity can objectively reflect the degree of insulin resistance in patients with type 2 diabetes mellitus.

Type 2 diabetes mellitus is a chronic low-grade inflammatory disease, and insulin has hypoglycemic, anti-inflammatory, vascular endothelial protection and various other effects. When insulin resistance occurs, the high blood glucose appears, activates the pro-inflammatory effect of macrophages, promotes fat cells to secrete a variety of adipocytokines and participates in the glucolipid metabolism and inflammatory reaction process[16,17]. Inflammatory adipocytokine is a new research field of diabetes and plays an important role in the development of diabetes mellitus, and the APN, LEP and SAA are the commonly studied at present. APN is the only hormone released by adipose tissue that has anti-inflammation, anti-diabetes and anti-atherosclerosis effects, the APN expression decreases in patients with coronary heart disease, and APN content can be an important means to evaluate the risk of coronary heart disease[18,19]. LEP shows negative feedback effect in insulin resistance and adipose tissue, the sensitivity of obese patients to LEP decreases, the negative feedback mechanism is damaged, and it cannot effectively inhibit islet  $\beta$  cells from secreting insulin, which results in hyperleptinemia and hyperinsulinemia[20]. SAA is an acute phase protein secreted by fat cells and its secretion increases in the inflammatory state. Current study has confirmed that the SAA level in serum of type 2 diabetic patients is higher than that of normal people[21]. The study showed that serum APN content in diabetes group was lower than that in normal control group whereas LEP and SAA contents were higher than those in normal control group, which is consistent with the physiological functions of each factor. Further Pearson test showed that ultrasonic carotid intima-media IMIsqrt and PWV levels in patients with type 2 diabetes mellitus were negatively correlated with APN content and positively correlated with LEP

and SAA contents, confirming that the ultrasonic carotid parameter levels can objectively reflect the degree of micro-inflammation in patients with type 2 diabetes mellitus, and indirectly reflect its illness severity.

The carotid intima-media unevenness and stiffness in patients with type 2 diabetes mellitus are higher than those in healthy people, and the specific increase is consistent with the degree of insulin resistance and micro-inflammation. The levels of ultrasonic carotid artery parameters can objectively reflect the disease severity of patients with type 2 diabetes mellitus, and can be used as one of the routine examinations for such patients in the future.

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