ORIGINAL ARTICLE

Insulin sensitivity in chronic pancreatitis and features of insulin resistance syndrome

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KEY WORDS

chronic pancreatitis, insulin sensitivity, pancreatic diabetes

ABSTRACT

INTRODUCTION Chronic pancreatitis predisposes to diabetes. Loss of endocrine function by β-cells in the Langerhans islets is considered to be the main causative factor, although several studies have also suggested insulin resistance as a possible additional mechanism.

OBJECTIVES The aim of the study was to estimate insulin sensitivity in chronic pancreatitis in view of the coexisting metabolic syndrome components.

PATIENTS AND METHODS The study involved 30 patients (mean age 50.83 ±6.61 years; 23.33% women, 76.66% men) diagnosed with chronic pancreatitis (using imaging tests). Insulin sensitivity with regard to the coexistent obesity, dyslipidemia, and arterial hypertension was measured using the euglycemic clamp method.

RESULTS Diabetes was present in 22 patients, impaired glucose tolerance in 4, and no carbohydrate metabolism disturbances in 4. Insulin resistance was present in 22 patients (73.33%), in whom a higher prevalence of diabetes (77.27% vs. 62.5%) and prediabetes (13.63% vs. 12.5%) was observed. The analysis of anthropometric parameters revealed that individuals with a high index of central obesity had a statistically significantly lower tissue glucose utilization (TGU) (3.23 vs. 4.89 mg/kg/min; $P = 0.02$), although there were no obese patients in the study group according to the body mass index. No statistically significant differences in TGU were observed in relation to lipid disorders (total cholesterol, low- and high-density lipoprotein cholesterol, triglycerides) and arterial hypertension.

CONCLUSIONS In patients with chronic pancreatitis, lack of correlation between insulin sensitivity and metabolic syndrome components may indicate that insulin resistance is related to primary disease or that an additional mechanism underlying pancreatic diabetes operates.

INTRODUCTION Diabetes secondary to chronic pancreatitis, also referred to as "pancreatic diabetes", is difficult to classify and treat. Progressive damage to the insulin-producing Langerhans islets is the most probable cause of secondary diabetes, and clinical and biochemical signs or symptoms usually occur when over 80% of the islets have been destroyed. Such injury is usually a result of prolonged fibrosis and calcification of pancreatic tissue, as well as inadequate blood flow into the pancreas as a consequence of chronic inflammatory process. Exo- and endocrine pancreatic cells are strictly controlled by both endocrine and gastrointestinal systems, constituting several regulatory pathways: entero-exocrine, entero-endocrine, and endo-exocrine. These regulatory circuits can be easily disturbed as a result of chronic pancreatitis, leading to the development of pancreatic diabetes.[1-3] A few reports have suggested that tissue insulin resistance can also play a significant role in the pathogenesis of secondary diabetes. So far, systemic and hepatic insulin resistance have been described. Insulin resistance has also been reported in chronic inflammatory processes, of which chronic pancreatitis is an example. Identification of an additional mechanism underlying abnormal carbohydrate metabolism in this patient group might help introduce new, more efficient therapeutic strategies and improve metabolic imbalance. Development of new treatment modalities is vital because the course of pancreatic diabetes is unstable, characterized

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TABLE 1 Mechanisms involved in pancreatic diabetes (secondary to chronic pancreatitis)

destruction of the Langerhans islets
fibrosis, calcification
inadequate blood flow resulting from chronic inflammation
disturbance of regulatory pathways
entero-exocrine
entero-endocrine
endo-exocrine
insulin resistance
systemic
hepatic

TABLE 2 Comparison of diagnostic criteria of metabolic syndrome according to the International Diabetes Federation (IDF) (2005) and Adult Treatment Panel III (ATP III) (2001)

Criterion	ATP III[a]	IDF[b]
abdominal obesity	W >88	W >80
waist circumference, cm	M >102	M >94
low HDL-C, mg/dl	W <50[c]	W <50[c]
	M <40[c]	M <40[c]
hypertriglyceridemia, mg/dl	>150[c]	>150[c]
elevated blood pressure, mmHg	>130/85[c]	>130/85[c]
fasting glucose, mg/dl	>110[c]	>100[c]

a 3 of 5 criteria required for the diagnosis
b abdominal obesity and 2 of 4 other criteria required for the diagnosis
c or previous diagnosis and treatment of: dyslipidemia, hypertension, or type 2 diabetes

Abbreviations: HDL-C – high-density lipoprotein cholesterol, M – men, W – women

TABLE 3 Characteristics of all patients included in the study

number of patients	30
mean age ±SD, yrs	50.83 ±6.61
age range, yrs	36–62
women, n (%)	7 (23.33)
men, n (%)	23 (76.66)
professionally active, n (%)	8 (26.66)
elementary education, n (%)	8 (26.66)
high-school education, n (%)	3 (10)
vocational education, n (%)	17 (56.66)
college graduates, n (%)	2 (6.66)
mean duration of CP ±SD, yrs	6.99 ±5.32
alcoholic etiology, n (%)	30 (100)
active alcoholism, n (%)	2 (6.66)
diabetes diagnosed prior to the study, n (%)	20 (66.66)
no history of AP, n (%)	7 (23.33)
history of at least 1 incident of AP, n (%)	14 (46.66)
history of 2 or more incidents of AP, n (%)	9 (30)
history of pancreatic cyst surgery, n (%)	16 (53.33)
history of pancreatic disease, n (%)	2 (6.66)
history of diabetes, n (%)	12 (40)
smoking at present, n (%)	25 (83.33)
smoking in medical history, n (%)	3 (10)

Abbreviations: AP – acute pancreatitis, CP – chronic pancreatitis, SD – standard deviation

by long, periods of severe hypoglycemia caused by impaired glucagon secretion.[1,4,5-8]

Possible etiological mechanisms of diabetes secondary to chronic pancreatitis are listed in TABLE 1.

When discussing insulin resistance, metabolic syndrome (also known as insulin resistance syndrome) should be mentioned. It is not considered as a separate disease entity, but rather as a cluster of risk factors for cardiovascular disease and type 2 diabetes. Metabolic syndrome includes abdominal obesity, elevated blood pressure, high triglyceride levels, low high-density lipoprotein (HDL) cholesterol levels, and impaired fasting plasma glucose. Prior diagnosis and treatment of diabetes, hypertension, or dyslipidemia allows to establish the presence of a particular risk factor. The comparison of 2 existing definitions of metabolic syndrome, the one published in 2001 by the Adult Treatment Panel III (ATP III) and a newer one, developed in 2005 by the International Diabetes Federation (IDF), reveals differences in the criteria used to assess abdominal obesity and fasting glucose levels (TABLE 2). The updated 2005 definition includes the race factor and identifies abdominal obesity as the waist circumference of at least 80 cm for women and 94 cm for men, as compared with 88 and 102 cm, respectively, in the ATP III guidelines. It seems that abdominal obesity, and not the total body fat, plays the most important role in the development of insulin resistance. As obesity becomes increasingly widespread, metabolic syndrome may emerge as the most common clinical syndrome associated with insulin resistance.[9-14]

The aim of the study was to determine insulin resistance in patients with chronic alcoholic pancreatitis using the euglycemic clamp method. Insulin resistance was assessed in the context of abdominal obesity, coexistent dyslipidemia and hypertension, as well as various carbohydrate metabolism disturbances.

PATIENTS AND METHODS A total of 30 patients diagnosed with chronic pancreatitis with or without carbohydrate metabolism disturbances were included in the study. Chronic pancreatitis had been previously diagnosed on the basis of ultrasonography or computed tomography. Morphological stage of the disease was evaluated on the basis of the widely accepted Cambridge classification. Functional and biochemical tests (e.g., elastase 1) were not performed, because of their overall negative effect on the body and limited usefulness in this particular study. All patients were supplemented with pancreatic enzymes, and at the time of the study, they did not report symptoms characteristic of the failure of pancreatic exocrine cells (steatorrhea, progressive weight loss). Diabetes had been previously diagnosed and treated in 20 of 30 patients (66.66%), a proportion reflecting preexisting epidemiological data. Characteristics of the patients are presented in TABLE 3. Diabetes diagnosed in patients prior to

TABLE 4 The course of diabetes in patients with chronic pancreatitis diagnosed prior to the study

Clinical parameter		Value
number of patients		20
mean age ±SD, yrs		50.1 ±6.57
age range, yrs		36–61
women, n (%)		4 (20)
men, n (%)		16 (80)
mean duration of diabetes ±SD, yrs		5.45 ±5.02
mean long-term control of diabetes ±SD (HbA_{1c}), %		9.03 ±2.14
treatment, n (%)	diet	2 (10)
	oral diabetes medications	1 (5)
	insulin	17 (85)
mean time on insulin ±SD, yrs		6 ±5.6
average daily dose of insulin ±SD, units		45.4 ±20.05
long-term complication, n (%)		8 (40)
coronary heart disease, n (%)		2 (10)
cerebrovascular disease, n (%)		0 (0)
peripheral artery disease, n (%)		2 (10)
retinopathy, n (%)		1 (5)
nephropathy, n (%)		0 (0)
neuropathy, n (%)		2 (10)
diabetic foot syndrome, n (%)		1 (5)

Abbreviations: see TABLE 3

the study was described as pancreatic (secondary, other); the course of the disease in each patient is detailed in TABLE 4.

Medical history was taken from all patients, and physical examination was performed, with an additional assessment of the oral cavity and detailed otolaryngological examination. Moreover, within 6 months prior to the study, all patients underwent imaging of the liver and pancreas (focal lesions, cirrhosis, etc.) as well as a number of biochemical tests on admission (TABLE 5). This allowed to exclude conditions that might have affected insulin resistance, such as inflammation, liver cirrhosis, advanced renal and heart failure, unstable coronary disease, and neoplastic disease.

In patients with chronic pancreatitis and normal carbohydrate metabolism, an oral glucose tolerance test was performed after a challenge with 75 g of glucose.[15]

Sensitivity to insulin was determined using the euglycemic clamp, which is a well-established reference method.[16] It is used to determine tissue consumption of glucose in response to artificially induced insulinemia. Under conditions of constant hyperinsulinemia, the amount of glucose utilized by tissues equals the amount of infused exogenic glucose, because after the first hour, the production of endogenous glucose becomes fully suppressed.

The test was performed using the TISS system developed in the Institute of Biostructure and Biocybernetics of the Polish Academy of Sciences in Warsaw, Poland. Normal tissue glucose utilization (TGU) was determined as higher than 5 mg/kg body weight/min on the basis of a test performed in healthy subjects in the past.[17] In our study, we decided not to perform the test for comparison either in healthy controls or patients with metabolic syndrome, because of its overall negative effect on the body. We agreed that the previously obtained results using the same system were sufficient to establish normal TGU values (an example of normal results is given in FIGURE 1).

Abdominal obesity was assessed using several anthropometric parameters, such as waist circumference (WC), interpreted according to the 2005 IDF guidelines, waist-to-hip ratio (WHR), and a relatively new index of central obesity (ICO), also known as waist-to-height ratio (WHtR). WHR lower than 0.8 for men and 1.0 for women was considered normal.[18,19] ICO, or WHtR, is calculated according to the formula: WC (cm)/height (cm); the normal values are: <0.51 for men and <0.47 for women.[20,21] The BMI was calculated according to the formula: body weight (kg)/height (m^2), with normal values ranging from 20 to 25 kg/m^2.[22-24]

Statistical analysis was performed using the STATISTICA 8.0 software. The Student's t-test for independent samples was used to determine statistical significance (P <0.05 considered as statistically significant). The analysis of variance was used for nonnormal distribution, ordinal

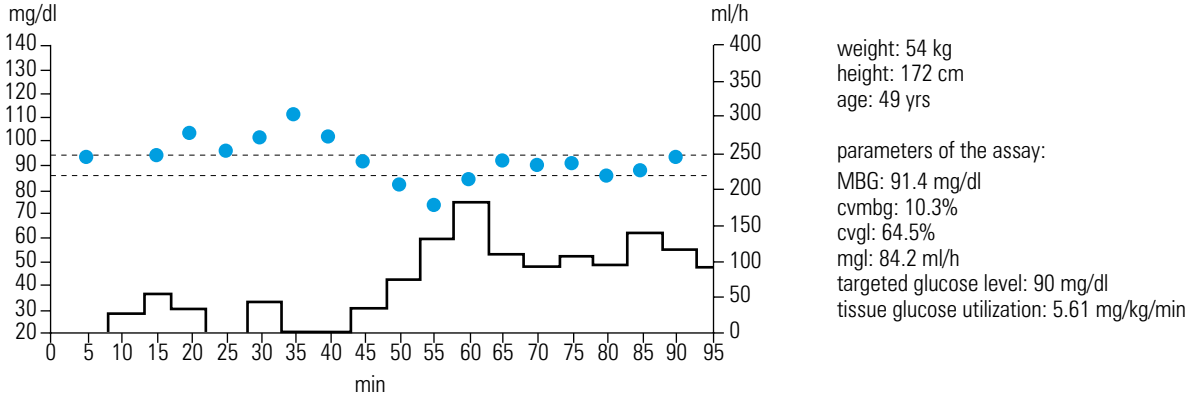

FIGURE 1 Example of a normal tissue glucose utilization result obtained using the euglycemic clamp
Abbreviations: MBG – mean bood glucose

TABLE 5 Laboratory tests performed prior to the study

erythrocyte count	alanine transaminase	pH
hematocrit	aspartate transaminase	O_2 pressure
hemoglobin concentration	bilirubin	CO_2 pressure
MCV	GGTP	bicarbonates
MCH	alkaline phosphatase	H ions
MCHC	LDH	lactates
leukocyte count	urea	HbA_{1c}
granulocytes, %	creatinine	prothrombin time
monocytes, %	uric acid	prothrombin index
lymphocytes, %	sodium	INR
platelet count	potassium	APTT
MPV	magnesium	fibrinogen
RDW	calcium	routine urine test
PCT	chlorides	color
diastase (serum)	phosphates	specific gravity
diastase (urine)	albumins	pH
lipase	α_1 globulins	glucose
TSH	α_2 globulins	protein
CA 19–9	β globulins	ketones
CEA	γ globulins	bilirubin
AFP	cholesterol	urobilinogen
iron	LDL-C	leukocytes
vitamin B_{12}	HDL-C	erythrocytes
ESR	triglycerides	bacteria
CRP	atherogenicity index	
folic acid	troponin	
ferritin	creatine kinase	
transferrin	creatine kinase mass concentration	

Abbreviations: AFP – α-fetoprotein, APTT – activated partial thromboplastin time, CEA – carcinoembryonic antigen, CRP – C-reactive sedimentation, ESR – erythrocyte sedimentation rate, GGTP – γ-glutamyltransferase, HbA_{1c} – glycated hemoglobin, INR – international normalized ratio, LDH – lactate dehydrogenase, LDL-C – low-density lipoprotein cholesterol, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, MCV – mean corpuscular volume, MPV – mean platelet volume, RDW – red blood cell distribution width, PCT – prothrombin consumption test, TSH – thyroid-stimulating hormone, others – see TABLE 2

data, and variance heterogeneity. Normal distribution of the variables, i.e., determining whether a given parameter is randomly selected from the population characterized by normal distribution, was assessed using the Shapiro-Wilk, Kolmogorov-Smirnov, and Lilliefors tests. Correlations were analyzed using the Pearson test for normal and the Spearman test for nonnormal distribution.[25]

RESULTS Insulin resistance was diagnosed in 22 patients (73% of the study group). A comparison between patients with insulin resistance and patients with normal TGU is presented in TABLE 6.

There was a negative correlation between BMI and TGU that was close to the level of statistical significance ($P = 0.07$). Of note, normal TGU was observed in only 1 patient from the group of subjects with BMI >25 kg/m^2 (FIGURE 2).

There was no statistically significant correlation between TGU and WC, although the comparison of mean TGU values between the groups with normal and high WC revealed higher values in the first one (FIGURE 3). Also, there was no statistically significant correlation between WC and TGU. Of all anthropometric parameters, the ICO was most useful in assessing insulin resistance in patients with chronic pancreatitis. Significantly higher TGU was observed in patients with normal ICO compared with those with higher ICO (4.89 ±1.75 vs. 3.23 ±2.11 mg/kg/min, respectively; $P = 0.02$; FIGURE 4). We did not observe any statistically significant differences in TGU when analyzing low and normal HDL cholesterol levels according to sex as well as increased and normal triglyceride levels, as recommended by the IFD in the diagnosis of metabolic syndrome (FIGURES 5 and 6).

Because insulin resistance is commonly associated with hypertension, TGU values in patients with and without hypertension were compared but no statistically significant differences were found (4.23 ±2.20 vs. 3.99 ±1.99 mg/kg/min, respectively; $P = 0.75$; FIGURE 7).

Prior to the study, 20 of 30 patients were diagnosed with diabetes (diabetes subgroup); the remaining 10 patients underwent a 75 mg glucose challenge (using the oral glucose tolerance test [OGTT]) that allowed to diagnose diabetes in 2 additional patients (newly diagnosed diabetes subgroup). The OGTT revealed prediabetes with impaired fasting glucose (IFG) in 4 patients (IFG subgroup), and normal carbohydrate metabolism (NCM) in 4 patients (NCM subgroup). All subgroups were compared with respect to their mean TGU. It was normal (>5 mg/kg/min) only in the NCM and IFG subgroups. The results are presented in FIGURE 8.

DISCUSSION With the increasing occurrence of obesity, insulin resistance has become a particularly important issue, with the result of there being much discussion as to whether it is useful to diagnose metabolic syndrome, which is an easy way to identify risk factors. Assessing insulin sensitivity, especially with the use of such a complicated and time-consuming method as the euglycemic clamp, is practically limited to scientific research. It is important to relate theses results to simple biochemical assays used in everyday clinical practice. Use of the BMI in anthropometric assessment of insulin sensitivity is worth considering. This simple parameter has long provided a quick and effective way to diagnose overweight and obesity, even though new parameters, described above, have been introduced.[22-24] Our study showed a strong negative correlation between BMI and TGU ($r = -0.33$), and although the significance level was low ($P = 0.07$), this relationship should not be ignored (FIGURE 2).

WC is one of the metabolic syndrome diagnostic criteria, and by many researchers it is considered as a requisite for determining insulin

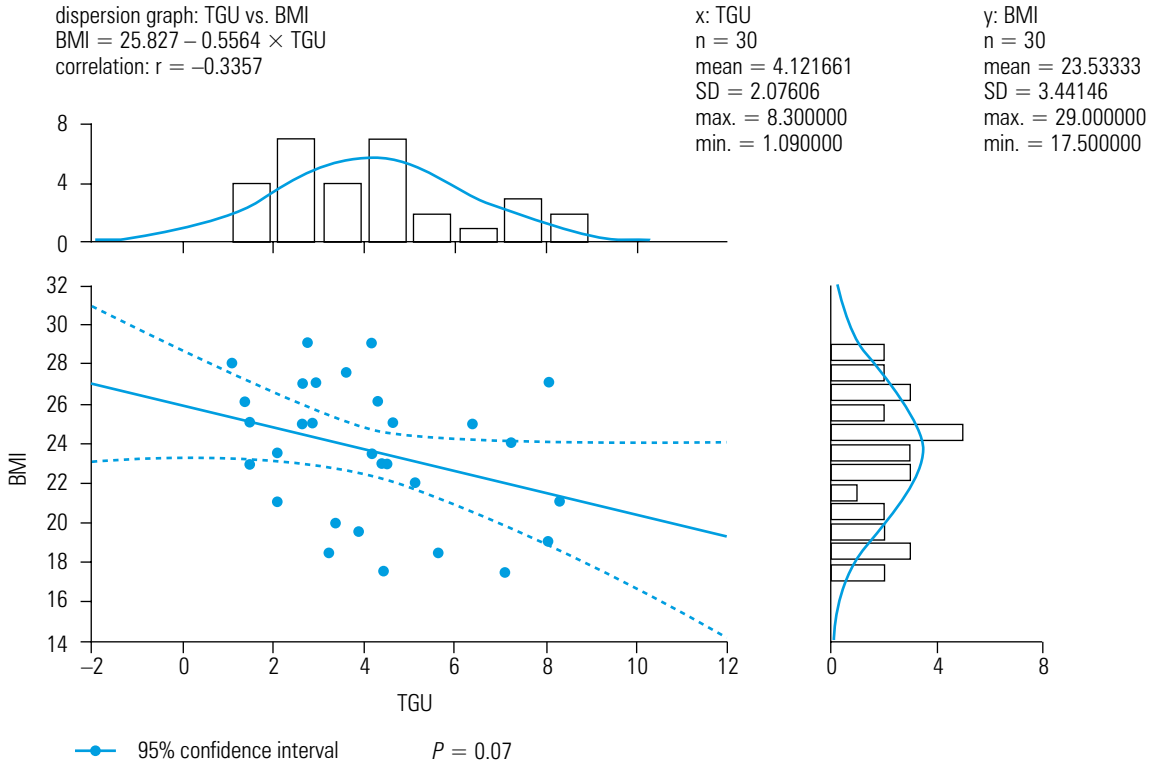

FIGURE 2 Correlation between tissue glucose utilization (TGU) and body mass index (BMI)
Abbreviations: see **TABLE 3**

TABLE 6 Comparison of patients with normal and decreased tissue glucose utilization

		Normal TGU	Low TGU/insulin resistance
number of patients, n (%)		8 (26.66)	22 (73.33)
mean age ±SD, yrs		50.12 ±5.51	51.09 ±7.07
age range, yrs		39–57	26–61
women, n (%)		2 (25)	5 (22.7)
men, n (%)		6 (75)	17 (77.3)
carbohydrate metabolism disturbances, n (%)	diabetes	5 (62.5)	17 (77.27)
	IFG	1 (12.5)	3 (13.63)
	none	2 (25)	2 (9.09)
mean HbA_{1c} levels ±SD, %		8.13 ±2.09	8.11 ±2.25
mean duration of diabetes ±SD, yrs		3.37 ±5.52	3.28 ±4.49
mean duration of CP ±SD, yrs		9.12 ±5.96	5.65 ±4.94
hypertension, n (%)		4 (50)	12 (54.54)
coronary heart disease, n (%)		1 (12.5)	3 (13.63)
peripheral artery disease, n (%)		1 (12.5)	1 (4.54)
retinopathy, n (%)		0 (0)	1 (4.54)
neuropathy, n (%)		1 (12.5)	1 (4.54)
diabetic foot syndrome, n (%)		1 (12.5)	0 (0)
mean total cholesterol levels ±SD, mg/dl		186.37 ±44.44	174.04 ±38.45
mean HDL-C levels ±SD, mg/dl		58.37 ±11.16	48.31 ±16.73
mean LDL-C levels ±SD, mg/dl		114.37 ±37.65	103.31 ±37.16
mean triglyceride levels, mg/dl		99.50 ±73.75	118.72 ±62.87

Abbreviations: see **FIGURE 2** and **TABLES 2, 3,** and **5**

resistance.[26-30] The comparison of TGU values between patients with normal WC and patients with abdominal obesity showed higher values in the first subgroup, although the differences were not statistically significant (4.51 ±2.21 mg/kg/min vs. 3.05 ±1.19 mg/kg/min; $P = 0.08$; **FIGURE 3**).

Recently, a number of studies emphasized the important prognostic value of the ICO.[20,31] Our study showed statistically significantly higher mean TGU values in patients with normal ICO as compared with those with elevated ICO. It should be highlighted that of all analyzed parameters,

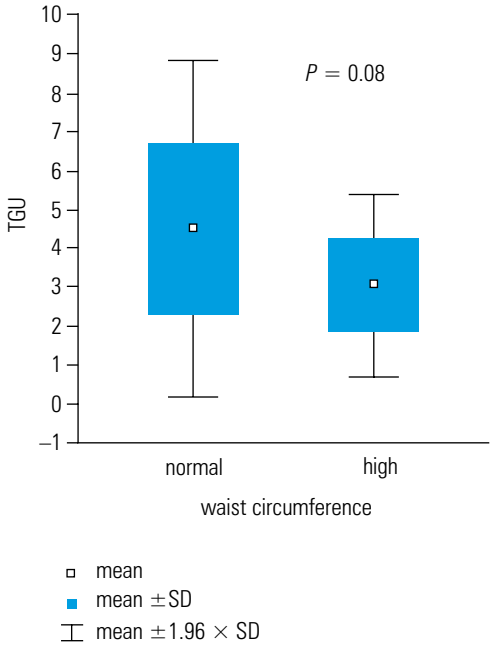

FIGURE 3 Mean tissue glucose utilization and waist circumference
Abbreviations: see FIGURE 2

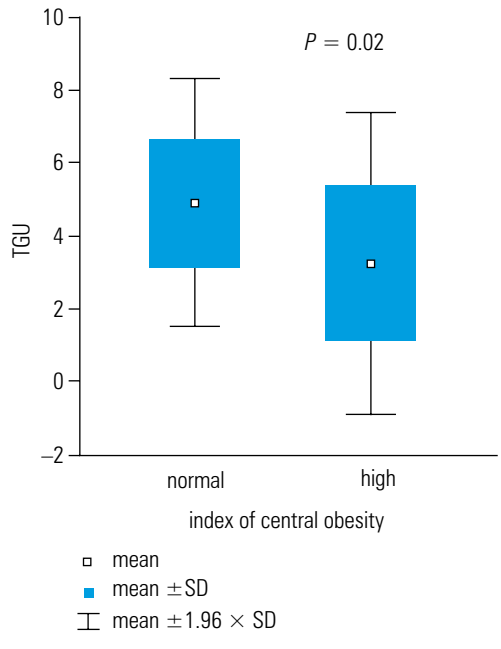

FIGURE 4 Mean tissue glucose utilization and the index of central obesity
Abbreviations: see FIGURE 2

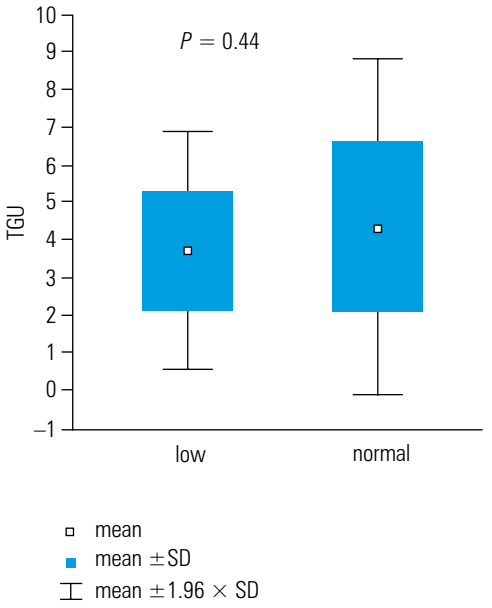

FIGURE 5 High-density lipoprotein cholesterol and tissue glucose utilization
Abbreviations: see FIGURE 2

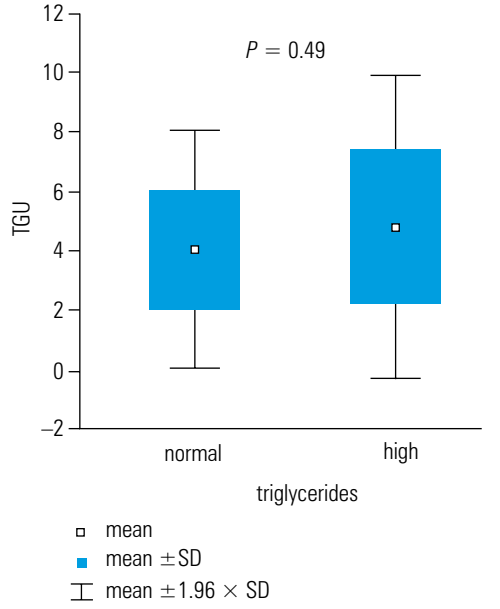

FIGURE 6 Triglyceride levels and tissue glucose utilization
Abbreviations: see FIGURE 2

only the ICO clearly showed a statistically significant correlation with TGU. Therefore, it may possibly become the most reliable, noninvasive indicator of insulin resistance in the future.

Dyslipidemia is one of the common features of metabolic syndrome. Hypertriglyceridemia is the most typical type of dyslipidemia, and it has been shown to correlate with a decrease in insulin sensitivity and coexist with elevated levels of low-density lipoprotein cholesterol and decreased levels of HDL cholesterol. The above abnormalities in blood lipid levels, together with insulin resistance, are directly linked to a significant increase in cardiovascular risk associated with atherosclerosis, and therefore are referred to as "atherogenic dyslipidemia".[32-34]

In our study, mean TGU values did not differ significantly between the subgroups of patients with chronic pancreatitis with low and normal HDL cholesterol and high and normal triglyceride levels (FIGURES 5 and 6). However, the results might have been biased by chronic pancreatitis

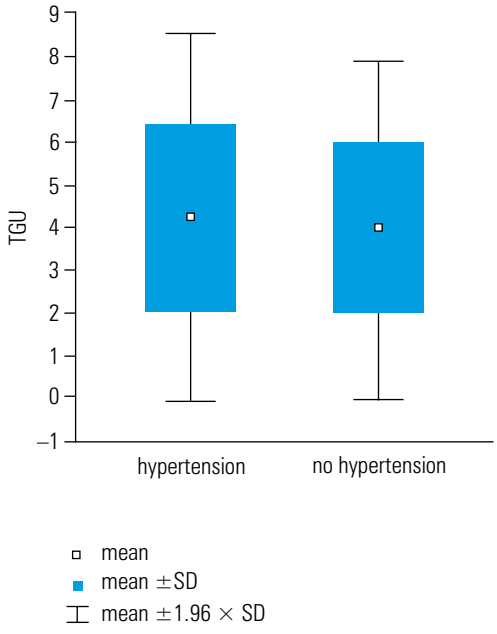

FIGURE 7 Tissue glucose utilization and arterial hypertensiona Abbreviations: see **FIGURE 2**

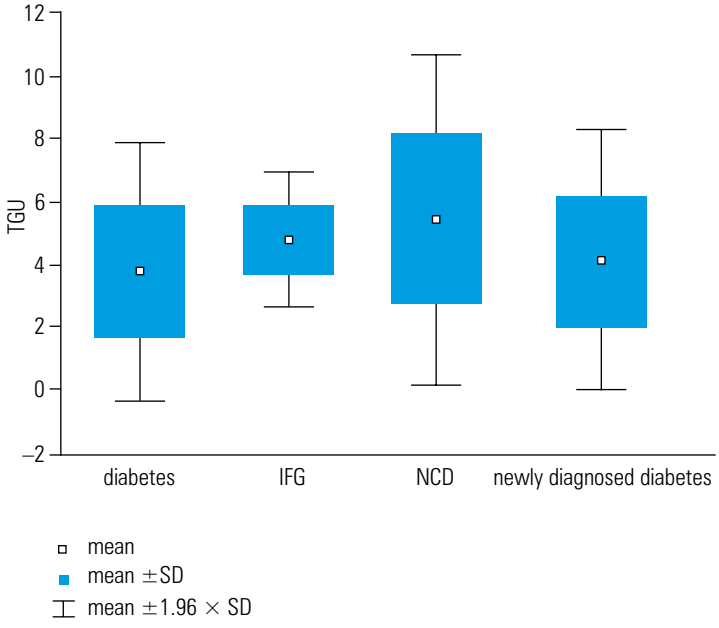

FIGURE 8 Tissue glucose utilization and various types of carbohydrate metabolism disturbances Abbreviations: IFG – impaired fasting glucose, NCM – normal carbohydrate metabolism, others – see **FIGURE 2**

and secondary disturbances of intestinal absorption resulting from impaired exocrine function.

Elevated blood pressure and/or previously diagnosed and treated hypertension are important components of metabolic syndrome. The association between hypertension and insulin resistance results from increased activation of both the renin-angiotensin-aldosterone pathway and sympathetic nervous system. This, in turn, is caused by an increased paracrine and endocrine activity of adipocytes in abdominal obesity as well as of secondary hyperinsulinemia.[35-38] We did not observe significant differences in the mean values of TGU between patients with hypertension and patients with normal blood pressure. Possibly, hypertension detected in this group of patients constitutes an independent, coexistent clinical disorder and is not a direct consequence of insulin resistance, as it was determined in the case of patients with dyslipidemia.

The analysis of the subgroups of patients characterized by various types of carbohydrate metabolism disturbances revealed the lowest mean TGU values in the diabetes subgroup (3.73 ±2.10 mg/kg/min) and highest in the NCM subgroup (5.42 ±2.67 mg/kg/min). Intermediate values were observed in the newly diagnosed diabetes and IFG subgroups (**FIGURE 8**). It may suggest that lower insulin sensitivity can accompany other carbohydrate metabolism disturbances present in chronic pancreatitis and act as an additional causative mechanism of these disturbances.

Conclusions Insulin resistance is detected in almost 75% of patients with chronic pancreatitis, despite the lack of obesity diagnosed on the basis of the BMI.

The ICO seems to be the most reliable anthropometric parameter that allows to detect insulin resistance in patients with chronic pancreatitis. We did not observe any correlations between lipid metabolism and insulin sensitivity. Coexistence of hypertension and chronic pancreatitis does not influence insulin resistance in any way. Lower insulin sensitivity, which is observed more often in patients with chronic pancreatitis and coexistent diabetes than in patients with normal carbohydrate metabolism, may suggest that the occurrence of insulin resistance syndrome is one of the mechanisms leading to the development of pancreatic diabetes.

REFERENCES

1 Romatowski JA, Stasiewicz J. Chronic pancreatitis: disturbances of endocrine function of pancreas. Medical Science Review. 2004; 3: 39-42.

2 Chang TM, Chey WY. Neurohormonal control of exocrine pancreas. Curr Opinion Gastroenterol. 2001; 17: 416-425.

3 Domschke S, Bloom SR, Adrian TE, et al. Chronic pancreatitis and diabetes mellitus: plasma and gastroduodenal mucosal profiles of regulatory peptides (gastrin, motilin, secretin, cholecystokinin, gastric inhibitory polypeptide, somatostatin, VIP, substance P, pancreatic polypeptide, glucagon, enteroglucagon, neurotensin). Hepatogastroenterology. 1988; 35: 229-237.

4 Szczeklik A, ed. [Internal diseases]. Vol 1. Kraków, Poland: Medycyna Praktyczna; 2005: 866-872.

5 Mohan V, Ramachandran A, Kumar GV, et al. Insulin resistance in Fibrocalculous (tropical) pancreatic diabetes. Horm Metab Res. 1988; 20: 746-748.

6 Cavallini G, Vaona B, Bovo P, et al. Diabetes in chronic alcoholic pancreatitis: role of residual beta cell function and insulin resistance. Dig Dis Sci. 1993; 38: 497-501.

7 Seymour NE, Turk JB, Laster MK, et al. In vitro hepatic insulin resistance in chronic pancreatitis in the rat. J Surg Res. 1989; 46: 450-456.

8 Yki-Järvinen H, Kiviluoto T, Taskinen MR. Insulin resistance is a prominent feature of patients with pancreatogenic diabetes. Metabolism. 1986; 35: 718-727.

9 Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel III). National Institute of Health. NIH Publication; 2002, 02-5215.

10 The IDF consensus worldwide definition of the metabolic syndrome. http://www.idf.org. Accessed April 15, 2005.

11 Pupek-Musialik D, Bryl W. [Metabolic syndrome – new guidelines, new challenges]. Przewodnik Lekarza. 2006; 6: 94-97. Polish.

12 Michael B, Elasy TA. [Clinical application of the definition of metabolic syndrome: what is the source of the doubts?] Diabetologia po Dyplomie. 2006; 3: 27-34. Polish.

13 Poirier P, Eckel RH. Obesity and cardiovascular disease. Curr Atheroscler Rep. 2002; 4: 448-453.

14 Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation. 1983; 67: 968-977.

15 [Clinical care practice for patients with diabetes 2008 – Guidelines of Polish Diabetes Association]. 2008; 9 (Suppl A): A1-A3. Polish.

16 Blachowicz J, Wójcicki J, Ładyżyński P, Krzymień J. [Measurement of tissue glucose utilization in human body]. Prace Instytutu Biocybernetyki i Inżynierii Biomedycznej. 1996; 48: 31-47. Polish.

17 Blachowicz J, Wójcicki J, Ładyżyński P, Krzymień J. [Measurement of tissue glucose utilization in human body]. Prace Instytutu Biocybernetyki i Inżynierii Biomedycznej. 1996; 48: 60-61. Polish.

18 Mohammed el A, Mohamed M, Denis L, Rekia B. Prevalence of parameter indicators of obesity and its relationship with metabolic syndrome in urban Moroccan women. Am J Hum Biol. 2008; 20: 484-486.

19 Reeder BA, Angel A, Ledoux M, et al. Obesity and its relation to cardio vascular disease risk factors in Canadian adults. Canadian Heart Health Surveys Research Group. CMAJ. 1992; 146: 2009-2019.

20 Cox BD, Whichelow MJ, Prevost AT. The development of cardiovascular disease in relation to anthropometric indices and hypertension in British adults. Int J Obes Relat Metab Disord. 1998; 22: 966-973.

21 Garnett SP, Baur LA, Cowell CT. Waist-to-height ratio: a simple option for determining excess central adiposity in young people. Int J Obes (Lond). 2008; 32: 1028-1030.

22 Rabkin SW, Chen Y, Leiter L, et al. Risk factor correlates of body mass index. Canadian Health Surveys Research Group. CMAJ. 1997; 157: S26-31.

23 McLaughlin T, Allison G, Abbasi F, et al. Prevalence of insulin resistance and associated disease risk factors among normal weight, overweight, and obese individuals. Metabolism. 2004; 53: 495-499.

24 Farin HM, Abbasi F, Reaven GM. Body mass index and waist circumference correlate to the same degree with insulin mediated glucose uptake. Metabolism. 2005; 54: 1323-1328.

25 Stanisz A. [A course in statistics using STATISTICA PL software and clinical medicine- based examples]. Vol 1. Kraków, Poland: StatSoft; 2006; 115-144, 221-234, 289-300. Polish.

26 Al-Lawati JA, Jousilahti P. Body mass index, waist circumference and waist-to-hip ratio cut-off points for categorization of obesity among Omani Arabs. Public Health Nutr. 2008; 11: 102-108.

27 Nyamdori R, Qiao Q, Soderberg S, et al. Comparison of body mass index with waist circumference, waist-to-hip ratio and waist-to-stature ratio as a predictor of hypertension incidence in Mauritius. J. Hypertens. 2008; 26: 866-870.

28 Dalton M, Cameron AJ, Zimmet PZ, et al. Waist circumference, waist-hip ratio and body mass index and their correlation with cardiovascular disease risk factors in Australian adults. J Intern Med. 2003; 254: 555-563.

29 Edwards LA, Bugaresti JM, Buchholtz AC. Visceral adipose tissue and the ratio of visceral to subcutaneous adipose tissue are greater in adults with than in those without spinal cord injury, despite matching waist circumferences. Am J Clin Nutr. 2008; 87: 600-607.

30 Narksawat K, Podang J, Punyarathabundu, et al. Waist circumference, body mass index and health risk factors among middle aged Thais. Asia Pac J Public Health. 2007; 19: 10-15.

31 Parikh RM, Joshi SR, Menon PS, Shah NS. Index of central obesity – a novel parameter. Med Hypotheses. 2007; 68: 1272-1275.

32 Lemieux I, Pascot A, Coilard C, et al. Hipertriglycerydemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia, hyperapolipoprotein B; small, dense LDL) in men? Circulation. 2000; 102: 179-184.

33 Rashid S, Watanabe T, Sakaue T, et al. Mechanisms of HDL lowering in insulin resistance, hypertrigliyeridemic states: the combined effect of HDL triglyceride enrichment and elevated hepatic lipase activity. Clin Biochem. 2003; 36: 421-429.

34 Fontbonne A, Eschwège EE, Cambien F, et al. Hypertriglyceridemia as a risk factor of coronary heart disease mortality in subjects with impaired glucose tolerance or diabetes: results from the 11-year follow-up of the Paris Prospective Study. Diabetologia. 1989; 32: 300-304.

35 Yki-Järvinen H, Utriainen T. Insulin-induced vasodilatation: physiology or pharmacology? Diabetologia. 1998; 41: 369-379.

36 Sechi LA. Mechanisms of insulin resistance in rat models of hypertension and their relationships with salt sensitivity. J Hypertens. 1999; 17: 1229-1237.

37 Scherer U, Sartori C. Insulin as a vascular and sympathoexcitatory hormone: implications for blood pressure regulation, insulin sensitivity, and cardiovascular morbidity. Circulation. 1997; 96: 4104-4113.

38 Berne C, Fagius J, Pollare T, Hjemdahl P. The sympathetic response to euglycemic hyperinsulinemia: evidence from microelectrode nerve recordings in healthy subjects. Diabetologia. 1992; 35: 873-879.

ARTYKUŁ ORYGINALNY

Insulinowrażliwość w przewlekłym zapaleniu trzustki a elementy zespołu insulinooporności

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SŁOWA KLUCZOWE

cukrzyca trzustkowa, insulinowrażliwość, przewlekłe zapalenie trzustki

STRESZCZENIE

WPROWADZENIE Przewlekłe zapalenie trzustki predysponuje do wystąpienia cukrzycy. Główną przyczyną jej powstawania jest utrata funkcji sekrecyjnej komórek β wysp trzustkowych, choć w piśmiennictwie istnieją doniesienia, że dodatkowym mechanizmem może być insulinooporność.

CELE Celem pracy była ocena insulinooporności w przewlekłym zapaleniu trzustki w aspekcie towarzyszących składowych zespołu metabolicznego.

PACJENCI I METODY W badaniu udział wzięło 30 chorych (średni wiek 50,83 ±6,61 lat; kobiety – 23,33%, mężczyźni – 76,66%) ze zdiagnozowanym przewlekłym zapaleniem trzustki (udokumentowanym w badaniach obrazowych). Określono insulinowrażliwość metodą klamry metabolicznej, w aspekcie typu zaburzeń gospodarki węglowodanowej oraz towarzyszących: otyłości, dyslipidemii oraz nadciśnienia tętniczego.

WYNIKI Cukrzycę stwierdzono u 22 pacjentów, u 4 – nieprawidłową glikemię na czczo, a 4 nie miało zaburzeń gospodarki węglowodanowej. Insulinooporność stwierdzono u 22 pacjentów (73,33%), u których w większym odsetku wystąpiła cukrzyca (77,27% *vs* 62,5%) oraz stan przedcukrzycowy (13,63% *vs* 12,5%). W analizie pomiarów antropometrycznych wykazano istotne statystycznie ($P = 0,02$) mniejsze średnie tkankowe zużycie glukozy (TZG) u osób z dużym wskaźnikiem otyłości brzusznej – 3,23 *vs* 4,89 mg/kg/min, choć w badanej grupie nie było pacjentów z otyłością określaną wskaźnikiem masy ciała. Nie stwierdzono również istotnych statystycznie różnic w zakresie TZG w zależności od poszczególnych elementów zaburzeń lipidowych (cholesterol całkowity, frakcji LDL i HDL, triglicerydy) oraz nadciśnienia tętniczego.

WNIOSKI Wśród chorych na przewlekłe zapalenie trzustki brak korelacji insulinooporności z głównymi składowymi zespołu metabolicznego może wskazywać na związek upośledzenia insulinowrażliwości z chorobą podstawową, bądź na dodatkowy mechanizm powstawania cukrzycy trzustkowej.

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