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Original Article

Comparative analysis of the structure and the function of the pancreas in patients with a combination of chronic pancreatitis and metabolic syndrome

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Abstract

In recent years, scientists are increasingly interested in the problem of influence of metabolic syndrome (MS) on gastrointestinal diseases. The aim of the study was to investigate the structure and the function of the pancreas in patients with a combination of chronic pancreatitis and metabolic syndrome. The higher BMI by 17.14%, waist circumference by 21.49%, WHR by 17.14%, WTR by 9.52%, WAR by 9.37%, WHtR by 30.00% have been found in patients with comorbid CBP and MS in comparison with the same in patients with isolated CBP ($p<0.05$).Among the patients with CBP, the liver stiffness index was (6.88±0.24) kPa and it was significantly higher by 30.2% than that in the control group ($p<0.05$). In patients with CBP+MS, the liver stiffness index was (7.70±0.15) kPa, which was higher by 37.6% and 10.6% than that in the control group and patients with CBP, respectively ($p<0.05$). The pancreas stiffness index was (7.08±0.11) kPa in patients with CBP and MS and it was higher by 34.0% and 8.6% compared to the same indexes in healthy people and those suffering from CBP, respectively ($p<0.05$). The concentration of fecal α-elastase 1 in patients with CBP+MS was (114.52±2.79) μg/g, which was significantly lower than the same in patients with CBP without MS (158.60±5.55) μg/g ($p<0.05$). The obtained results proved an aggravating effect of comorbid metabolic syndrome on the structure of the liver and on the structure and function of the pancreas in patients with chronic biliary pancreatitis.

Keywords: chronic pancreatitis, metabolic syndrome, comparative analysis, structure of pancreas, function of pancreas.

Introduction

In recent years, scientists are increasingly interested in the problem of influence of metabolic syndrome (MS) on gastrointestinal diseases [1, 2]. This research direction is important and relevant, since pathological changes in the liver and the pancreas in MS, contribute to the progression of it and the development a lot of complications.

The prevalence of MS is quite high [2, 3]. Experts estimate that the number of adults with MS is 25–40% [3]. In industrialized countries, the prevalence of MS among the population over 30 years old is 10–20% [4].

Insulin resistance (IR) is the main factor contributed to MS [3, 5]. IR is a prognostic factor in the development of a number of diseases (ischemic heart disease, diabetes mellitus, hypertension), as well as an independent factor in the development of atherosclerosis [4–6]. In many cases, excess body weight is the trigger for IR [7].

Metabolic syndrome (MS) is a complex of metabolic, hormonal, and clinical disorders that are linked by common pathogenetic links [6, 8].

About 15% of all people aged 40 to 75 years suffer from chronic pancreatitis (CP) [9–13] in combination with MS (impaired glucose tolerance or diabetes mellitus (DM) type 2, abdominal obesity, dyslipidemia, arterial hypertension, hyperuricemia, microalbuminuria etc) [14, 15].

As the pancreas has exocrine and endocrine functions, it takes part in many physiological processes [16–18].

The unique value of the pancreas is producing a number of hormones, which are opposite in action and closely interact with each other, maintaining homeostasis in a dynamic equilibrium [2]. Therefore, diseases of the pancreas, including chronic pancreatitis (CP), are considered as diseases that affect on the exocrine and endocrine parts of the organ, which leads to homeostasis violation, metabolic disorders [19]. Endocrine insufficiency leads to the manifestation of metabolic disorders; and damage of acinar cells and pancreas ducts correlates with a endocrine dysfunction [7]. Therefore, a violation of the interrelationships of these pancreas functions can lead to chronic pancreatitis (CP), while the cause will be metabolic disorders that lead to IR and compensatory hyperinsulinemia [2, 20, 21].

Comorbid pathologies complicate each other's clinical course, leads to difficulties in diagnosis and a treatment strategy, and significantly worsen the patient's quality of life [5, 22]. An important clinical and social problem is the necessity of improving diagnosis and treatment of diseases associated with MS, as they lead to early disability and high mortality [1, 4, 23, 24].

The aim of the study was to investigate the structure and the function of the pancreas in patients with chronic pancreatitis and metabolic syndrome.

Material and methods

A number of 137 patients with chronic biliary pancreatitis (CBP) were examined. Patients were divided into 2 groups: the main group included 115 patients with CBP in combination with MS; the comparison group included 22 patients with isolated CBP. Control group consisted of 20 practically healthy people.

The average age of the patients was (52.4±3.2) years. The patients were representative in terms of age, sex, disease duration, and socio-economic conditions. Examination of patients was carried out with their consent. The average duration of CBP was (7.7±2.4) years. The presence of MS was assessed according to the guidelines of the National Heart, Lung and Blood Institute (NHLBI) and the American Heart Association (AHA) in which at least 3 of the 5 MS criteria were diagnosed (increased waist circumference, elevated serum triglycerides (TG), decreased high-density lipoprotein (HDL), fasting hyperglycemia, high blood pressure). The diagnosis of CP was based on Marseille-Cambrige classification.

The structure of the liver and the pancreas was estimated by shear wave elasticity imagining (SWEI) using ultrasound device Ultima PA ("Radmyr", Kharkiv, Ukraine) with a linear detector on frequency of 2–5 MHz at depth of 10–50 mm.

Inclusion criteria in research study: presence of CP of biliary genesis, body mass index (BMI) over 30.0 kg/m^2, the ratio of waist circumference to hip circumference (WC/HC) over 1.0 for men and 0.8 for women, hypertension and/or carbohydrate metabolism disorders.

Exclusion criteria in research study: diabetes mellitus requiring insulin and drug therapy, hepatitis and cirrhosis, including viral etiology, oncology, decompensated pathologies, patients' refusal to participate in research study.

The study was conducted according to World Medical Association Declaration of Helsinki "Ethical principles for medical research involving human subjects" by the decision of the Ethics Committee of I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine (protocol № 6/2021).

The blood glucose level and HbA1c were calculated according to generally accepted criteria. HOMA-IR was calculated according to the formula:

$$\text{HOMA-IR} = \text{fasting insulin} \times \text{fasting glucose}/22.5 \quad (1)$$

The following obesity indices were used [25, 26]:

- WHR (waist-hip ratio). WHR is the ratio of the circumference of the waist to that of the hips. Normal WHR is <0.85 for women and <1.0 for men;
- WTR (waist-thigh ratio). WTR is the ratio of the circumference of the waist to that of the thigh. Normal WTR is <1.5 for women and <1.7 for men;
- WAR (waist-arm ratio). WAR is the dimensionless ratio of the circumference of the waist to that of the arm. Normal WAR is <2.4 for all people;
- WHtR (waist-heigh ratio). WHtR is the dimensionless ratio of the circumference of the waist to the heigh. Normal WHtR is <0.5 for all people.

Fecal elastase-1 was evaluated by enzyme-linked immunosorbent assay using ELASTASE 1-ELISA kits (BIOSERV). The severity of exocrine pancreatic insufficiency (EPI) was evaluated according to the fecal elastase-1 level: severe EPI – <100 μg/g; moderate EPI – 100–150 μg/g; mild EPI – 150–200 μg/g; normal pancreatic function (without EPI) is considered when fecal elastase-1 level is >200 μg/g.

Statistical processing of the obtained research data was processed using the software Excel (Microsoft, USA) and Statistica.10.1 (StatSoft USA), using the Mann-Whitney U-test and the Student's test (t). When

Table 1: Comparative analysis of glucose metabolism parameters of patients with CBP and MS.

Glucose metabolism parameter	Groups of comparison		
	Control group (n=20)	CBP (n=22)	CBP+MS (n=115)
Fasting blood glucose, mmol/l	4.70±0.11	5.31±0.12*	5.99±0.29**
HbA1c, %	4.55±0.11	5.47±0.15*	6.10±0.14**
HOMA-IR	1.47±0.07	1.84±0.09	2.60±0.10**

Note: * – statistically significant difference between index in CBP and MS group, CBP group compared to that in the control group ($p<0.05$); ** – statistically significant difference between index in CBP and MS group compared to that in CBP group ($p<0.05$).

a P-value was less than 0.05, the results were considered statistically significant.

Results

Table 1 shows the parameters of glucose metabolism, which can be used to characterize the endocrine function of the pancreas in patients with CBP and MS.

The statistically significant higher HbA1c level was found in patients with CBP and comorbid MS compared to the same in patients with CBP [(6.10±0.14) % *vs.* (5.47±0.15) %]. Also, the significantly higher HbA1c level was found in patients with isolated CBP compared to that in the control group, which with a high degree of probability can indicates on high risk of the developing of pre-diabetes, while in patients with CBP+MS the HbA1c level was between 5.7% and 6.4%, which is considered pre-diabetes. Also the significantly higher blood glucose level was established in patients with CBP+MS [(5.99±0.29) mmol/l compared to the same in patients with CBP (5.31±0.12) mmol/l]. ThesSignificantly higher HOMA-IR was also found in patients with CBP+MS compared to the same in patients with CBP ($p<0.05$) – 2.60±0.10 *vs.* 1.84±0.09.

The significantly higher HOMA-IR level was also found in patients with CBP+MS compared to the same in patients with CBP (2.60±0.10 *vs.* 1.84±0.09, $p<0.05$). HOMA-IR level in patients with CBP+MS was abnormal (optimal values are considered to be 1.7–2.0), which confirmed the presence of IR in patients with comorbidity, while in patients with isolated CBP this parameter was normal. Table 2 shows anthropometric parameters of patients with CBP and MS.

The significantly higher BMI, waist circumference, and abdominal obesity indices were found in patients with CBP+MS compared to the same in patients with CBP ($p<0.05$).

The higher BMI by 17.14%, waist circumference by 21.49%, WHR by 17.14%, WTR by 9.52%, WAR by 9.37%, WHtR by 30.00% have been found in patients with comorbid CBP and MS in comparison with the same in patients with isolated CBP ($p<0.05$).

Table 2: Anthropometric parameters of patients with CBP and MS.

Parameter	Normal range	Control group (n=20)	Groups of comparison	
			CBP (n=22)	CBP+MS (n=115)
BMI, kg/m²	18.5–24.9	23.46±0.68	25.58±1.06	31.84±0.34**
Waist circumference, cm	≤94 in men ≤80 in women	77.30±2.59	79.76±1.79	101.60±0.82**
WHR	<1.0 in men <0.85 in women	0.79±0.01	0.87±0.02	1.05±0.02**
WTR	<1.7 in men <1.5 in women	1.60±0.03	2.09±0.03*	2.31±0.04**
WAR	<2.4	2.45±0.03	2.90±0.02*	3.20±0.01**
WHtR	<0.5	0.45±0.01	0.42±0.02	0.60±0.01**

Note: * – statistically significant difference between index in CBP and MS group, CBP group compared to that in the control group ($p<0.05$); ** – statistically significant difference between index in CBP and MS group compared to that in CBP group ($p<0.05$).

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Table 3: Indices of liver stiffness and pancreas stiffness in patients with CBP and MS.

SWEI index	Control group (n=20)	Groups of comparison	
		CBP (n=22)	CBP+MS (n=115)
Liver, kPa	4.80±0.24	6.88±0.24*	7.70±0.15***
Pancreas, kPa	4.67±0.32	6.47±0.29*	7.08±0.11**

Note: * – statistically significant difference between index in CBP and MS group, CBP group compared to that in the control group ($p<0.05$); ** – statistically significant difference between index in CBP and MS group and that in CBP group ($p<0.05$); *** –statistically significant difference between the liver stiffness index and the pancreas stiffness index in patients with CBP+MS ($p<0.05$).

All of the above indicate on the presence of excess body weight and obesity in patients with CBP, which was more significant in those patients with MS.

In addition to standard ultrasound, the structure of the liver and the pancreas, was estimated by share wave elasticity imaging- SWEI (Table 3).

In the control group, the liver stiffness index and pancreas stiffness index were (4.80±0.24) kPa and (4.67±0.12) kPa, respectively. That's mean that the structure of the liver and the pancreas had no changes.

Among the patients with CBP, the liver stiffness index was (6.88±0.24) kPa and it was significantly higher by 30.2% than that in the control group ($p<0.05$). In patients with CBP+MS, the liver stiffness index was (7.70±0.15) kPa, which was higher by 37.6% and 10.6% than that in the control group and patients with CBP, respectively ($p<0.05$). The pancreas stiffness index was (7.08±0.11) kPa in patients with CBP and MS and was higher by 34.0% and 8.6% compared to the same indexes in healthy people and those suffering from CBP, respectively ($p<0.05$).

It was also found that the liver stiffness index was significantly higher than the pancreas stiffness index ($p<0.05$) in the patients with CBP and MS.

The concentration of fecal α-elastase 1 in patients with CBP+MS was (114.52±2.79) μg/g, which was significantly lower than the same in patients with CBP without MS (158.60±5.55) μg/g ($p<0.05$).

Discussion

The increased blood glucose level and HbA1c indicate the aggravating role of MS on the formation of endocrine insufficiency in patients with chronic pancreatitis and motivates for early investigation of DM markers in CBP in combination with MS. The significantly higher HOMA-IR level in patients with CBP+MS compared to that in patients with isolated CBP confirms the presence of IR in patients with the comorbidity.

Patients with CBP and MS had significantly increased stiffness indices of both the pancreas and the liver ($p<0.05$) in comparison with such patients without comorbid MS. The presence of comorbid MS not only aggravated the course of CBP, but also led to an increased structural damage of the liver and the pancreas and their influence on each other.

In patients with CBP and MS, the pancreas stiffness index was significantly lower than that of the liver ($p<0.05$), which indicates more severe damage of liver parenchyma compared to the pancreas parenchyma.

Assesment of exocrine function of the pancreas showed a mild degree of EPI in patients with CBP while medium degree in patients with CBP and comorbid MS. More severe EPI in patients with CBP and MS compared to the those patients without MS ($p<0.05$) indicates the aggravating effect of MS on the course of CP.

Conclusions

It was established that glucose metabolism disorders were more severe in the patients with chronic biliary pancreatitis combined with metabolic syndrome compare with those without obesity by the level of fasting blood glucose, HbA1c and HOMA-IR (by 11.54%; 10.32% and 29.23%, respectively), which proved more severe endocrine dysfunction in formation of diabetes mellitus in combination of chronic pancreatitis and metabolic syndrome.

It was established significantly higher BMI, waist circumference, and indices of abdominal obesity which indicate the presence of fat metabolism disorders, excess body weight and abdominal obesity in patients with chronic biliary pancreatitis and metabolic syndrome.

More significant structural disorders of the liver and the pancreas (increased stiffness indexes by 10.64% and 8.61%, $p<0.05$, respectively) were established (according to share wave elasticity imaging data) in patients

with chronic biliary pancreatitis with comorbid metabolic syndrome.

It was established more severe exocrine pancreatic insufficiency in patients with chronic biliary pancreatitis and metabolic syndrome compared to those without metabolic syndrome by the level of fecal α-elastase 1 (by 27.8%, $p<0.05$).

The obtained results proved an aggravating effect of comorbid metabolic syndrome on the structure of the liver and on the structure and function of the pancreas in patients with chronic biliary pancreatitis.

Conflict of interest

The authors declare no conflict of interest.

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