DYSFUNCTION OF THE LEFT VENTRICLE IN PATIENTS WITH CHRONIC PANCREATITIS CAUSED BY ALCOHOLISM

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The aim of the study was to determine systolic and diastolic left ventricular function in the patients with chronic pancreatitis.

Sixten patients with chronic alcoholic pancreatitis (12 male and 4 female; 43±7 years old; 11 with diabetes) and 15 healthy controls (8 male and 7 female; 37±9 years old) were inclouded in the study. No one had any clinical signs of heart disease. Using two-dimensional echocardiography, in patients and controls we estimated: end diastolic diameter (EDD); end systolic diameter(ESD); ejection fraction (EF) and fractionar shortening (FS). By Doppler echocardiography we measured the peak early and artrial filling velocities and their ratio as well.

In patients with chronic pancreatitis systoliuc function was preserved since diastolic dysfunction was reveled (VA in patients versus VA in controls: 0,66±0,13 vs. 0,45±0,05 $p<0,05$; VE/VA ratio in patients versus VE/VA in controls: 0,91±0,3 vs. 1,3±0,3 $p<0,05$).

We can consider diabetes mellitus, major complication of chronic pancreatitis as the primarly cause of left ventricular diastolic dysfunction.

Key words: left ventricular function, chronic pancreatitis

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In spite of the fact that the first description of chronic pancreatitis was published more than two centuries ago, this disease has remained, till these days, an enigma due to vague pathogenesis, unpredictable clinical course and indefinite treatment.

Morphological changes characteristic for chronic pancreatitis include variable extent of fibrosis, inflammation and exocrine function loss /1/. Clinically, chronic pancreatitis is silent in a large number of patients. In addition, a certain number of patients with inexplicable abdominal pain may have chronic pancreatitis. For this reason, the incidence rate of the disease is unreliable and ranges from 0.04 to 5% /1/.

The origin of chronic pancreatitis is vague in 10% to 20% of the affected persons /2/. The most recognized cause of chronic pancreatitis is alcoholism. It is believed that perennial consumption of large volumes of alcoholic beverages (150g to 175g/day) is the cause of pancreatitis in 70% to 80% of cases /1,2/. The obstruction of pancreatic duct is one of well-known causes of chronic pancreatitis. It may be posttraumatic; it may be caused by pseudocysts,

mechanical structural changes of ductal sphincter as well as periampullar tumors. Rare forms of so-called tropical pancreatitis of unknown origin are seen in African and Asian regions (probably due to hypoproteinemia or intake of toxic substances). Pancreatitis may occur either in association with cystic fibrosis and hyperparathyroidism or as autosomal dominant hereditary disease.

Protein hypersecretion from the acinic cells without adequate increase of bicarbonate secretion is characteristic for chronic pancreatitis. Consequently, interlobular and intralobular plugs resulting from protein precipitation are found rather early. Ductal plugs are initially composed of degenerative cells within the reticular net. They are enlarged by laminar aggregates and amorphous substances. The plugs contain proteins including digestive enzymes, glycoproteins and mucopolysaccharides. Calcium carbonate precipitation results in formation of intraductal calculi. The finding of small ductal calculi is pathognomonic for alcohol-induced chronic pancreatitis.

Therefore, all the aforementioned lead to inevitable progressive deficit of pancreatic parenchyma. Following the subacute phase of varying length, the attacks of abdominal pain are being repeated with the subsequent exocrine and endocrine insufficiency, occurring in 15% to 20% of patients /3/. Fundamental manifestation of endocrine insufficiency is diabetes mellitus that may give rise to modifications of almost all organs and organ systems /2,3/. Resulting neuropathy, micro- and macrovascular changes promote to a large extent the increase of total morbidity and mortality of patients with chronic pancreatitis.

Cardiovascular system changes associated with chronic pancreatitis as well as consequent complications have not been the issue of general interest. In 1980s of the last century, several studies on ECG changes in patients with chronic pancreatitis were published /4,5/. Structural and functional changes of myocardium in patients with chronic pancreatitis were not the subject of study. In accordance with echocardiography options, the objective of this study was to define the systolic and diastolic function of the left ventricle in patients with chronic pancreatitis.

Patients and methodology

The study included 16 patients with chronic pancreatitis (12 males and 4 females, mean age 43±7) and 15 healthy controls (8 males and 7 females, mean age 37±9 years). The history of all patients revealed perennial consumption of alcohol (≥50g/day). Diabetes mellitus was found in 11 patients. No one of patients and controls had clinical manifestations of cardiac condition.

Diagnosis of chronic pancreatitis was based on clinical picture of repeated waist pains, steatorrhoea, and X-ray and echotomography or CT scanning.

The patients and the controls underwent conventional echocardiography to determine end-diastolic diameter (EDD) and end-systolic diameter (ESD) of the left ventricle. By means of these values and using Teichholz formula, the volumes as well as the ejection fraction (EF) and fraction shortening (FS) of the left ventricle were determined. Doppler echocardiography was used to determine the maximum velocity of the early diastolic filling of the left ventricle (VE) and flow caused by atrial contraction (VA) as well as their ratio (VE/VA).

Results

As illustrated in Table 1, there was no significant difference of the left ventricle diameters, thickness of free wall and interventricular septum, as well as the ejection fraction and fraction shortening between the patients with chronic pancreatitis and healthy controls.

	Patients	Controls	Significance
EDD	5,3±0,4	5,0±0,5	n.s.
ESD	3,8±0,3	3,4±0,3	n.s.
IVS	1.08±0,02	1,01±0,04	n.s.
PW	0,98±0,04	0,91±0,08	n.s.
EF	62±8	66±8	n.s.
FS	29±6	30±4	n.s.

Table 1. The illustration of diameters and parameters of the left ventricle function in patients and controls

The analysis of variance of transmitral flow parameters revealed significantly higher velocity of A waves of atrial contraction in the group of patients with chronic pancreatitis in relation to healthy controls. The flow rate ratio (E/A) was significantly lower in patients than in healthy controls, as presented in Table 2.

	Patients	Controls	Significance
VE(m/s)	0,62±0,16	0,6±0,15	n.s.
VA(m/s)	0,58±0,13	0,45±0,05	$p<0,05$
E/A	1,1±0,3	1,3±0,3	$p<0,05$

Table 2. Doppler parameters of diastolic function of the left ventricle in patients and controls

Discussion

In patients with chronic pancreatitis, it is difficult to distinguish the effect of diabetes mellitus, as a complication of chronic pancreatitis, from the ethylism, as its cause, to the structural and functional changes of cardiovascular system /6/.

It is well-known that the patients with chronic pancreatitis, in their terminal phase of the disease, and predominantly as the sequleae of diabetes mellitus, may develop autonomous cardiac dysfunction which is manifested as lower accommodation of heart rate at rest and in stress test /3,7/. Resting tachycardia may arise due to generalized reduction of effect of parasympathetic nervous system to modulation of heart rate. In addition, the changes of circadian rhythm with predominant activity during night and ventricular extrasystoles may also occur, what all increase the risk of sudden death in these patients. Such disorder is verified by 24-hour measurement of heart rate variability. In hospital conditions, time-determined variability of heart rate is tested by different respiratory maneuvers /3/.

Geller and associates named the presence of arrhythmia (extrasystole arrhythmia), vascular hypotonia and lower ECG voltage within chronic pancreatitis as the “pancreatocardiac syndrome” /8/. The same authors found that dysrhythmia developed in about 70% of patients with chronic pancreatitis. They tried to explain these changes by metabolic disorders of biogenic amines and lower insulin level /8/.

Two decades ago, Gulo and associates proved higher incidence of coronary disease in patients with chronic pancreatitis, and its manifestation in younger age /4/. Similar, Mansake and associates found that 88% of patients with chronic pancreatitis, complicated by diabetes mellitus, and over 45 years of age, had at least one critical stenosis of coronary arteries /9/. Metabolic disorders in chronic pancreatitis are assumed to favor earlier and more frequent development of coronary disease. Moreover, evident coagulation disorders and electrolytic imbalance might contribute to coronary disease in patients having chronic pancreatitis /10/. Furthermore, chronic pancreatitis is associated with intractable increase of free radicals oxidation, especially in older persons, what is again associated with higher incidence of coronary disease /11/.

Epidemiological studies verified that high frequency of primarily diastolic and not so often systolic dysfunction of the left ventricle was characteristic for patients with diabetes mellitus. Conventional echocardiography and Doppler echocardiography provided reliable detection of these complications. Diastolic dysfunction has been found in even 50% of the affected /11/. Based on the experimental studies, it may be assumed that underlying condition of diastolic disorder of the left ventricle in diabetes mellitus patients is the impaired myocyte calcium turnover along with microvascular changes /12/. In the studied group of patients, the apparent diastolic malfunction may be explained by metabolic disorders, that is, diabetes mellitus that was present in 64% of patients. The obtained abnormal pattern of transmitral flow, where VE/VA ratio was less than 1, was the indicator of slow relaxation of the left ventricle what was the explicit sign of diastolic dysfunction of the left ventricle. No impairment of systolic function of the left ventricle was found in the group of patients. Belzer and collaborators obtained similar results. They ruled out the association of systolic interval changes and chronic pancreatitis /12/. Such finding of unaltered systolic function of the left ventricle was surprising because of well-known role of ethylism in the origin of alcoholic cardiomyopathy.

On the basis of medical history of studied patients, it could be concluded that the cause of pancreatitis was the alcohol consumption. It is known that the exposure to ethanol results in reduction of synthesis of mitochondrial proteins, affecting the development of cardiomyopathy /13/. Free radical- induced oxidative stress may have a role in pathogenesis of ethanol-related cardiac abnormalities.

Other than structural changes, alcohol causes primarily the impairment of systolic function of the left ventricle. There are no available data on diastolic dysfunction of the left ventricle in ethylics.

The conclusion may be drawn that, in our studied patients with chronic pancreatitis, the existing diastolic dysfunction of the left ventricle was caused by diabetes mellitus as the complication of the underlying disease, and, in spite of ethylic origin of chronic pancreatitis, no systolic dysfunction of the left ventricle was recorded.

Clinical significance of the study was to detect asymptomatic diastolic dysfunction in patients with chronic pancreatitis. Prognostic value of our study will be estimated by follow-up of these patients.