



Gender Features of Cardiac Manifestations in Calculous Cholecystitis

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Abstract

The incidence of gallstone disease among female patients is higher than among men. Various studies show that 10.5% of cases among women with cholelithiasis have a history of cardiac manifestations, and the prevalence of cardiovascular pathology in the absence of calculous cholecystitis is 11.9%. The purpose of this study is to study the relationship of gender characteristics with cardiac manifestations of calculous cholecystitis. 80 patients aged 37-70 years with pathology of the biliary and cardiovascular systems were examined. The study participants were divided into groups of 40 people depending on gender. The control group consisted of patients with pathology of the cardiovascular system. All patients underwent a comprehensive examination using clinical, laboratory, and instrumental research methods.

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1 Introduction

The modern rhythm of life is closely associated with a violation of the diet and diet, physical inactivity, and high emotional stress, which can lead to metabolic disorders and the appearance of diseases. Currently, the most common disease is cholelithiasis (calculous cholecystitis). The number of patients with diseases of the biliary tract increases every year [1,2].

The greatest number of diseases were detected in developed countries and in residents of large industrial cities. At the same time, the incidence of calculous cholecystitis in women is higher than in men. According to surveys, gallstones are diagnosed in 70% of women and 30% of men, with 5-30% of women aged 20 to 50 years, 25-40% over 50 years. In men, these indicators are lower [3].

Cholecystitis is an inflammation of the gallbladder. With calculous cholecystitis, stones (bile concretions) form in the ducts of the gallbladder, they disrupt its normal patency, causing stagnation of bile and inflammation. The basis of stone formation is a prolonged stagnation of bile, the inability of bile to retain cholesterol, which settles in the gallbladder and ducts in the form of crystals or "sand", the crystals stick together and form stones, and various components of bile (salts, pigments) stick to them [4,5].

Risk factors for cholelithiasis have gender and age-specific feature. Among the main risk factors are the following:

1. Female gender: menstrual disorders, oral contraceptives and estrogen replacement therapy, frequent pregnancies and childbirth lead to a change in the hormonal background of a woman, increase the level of estrogens, reduce the level of bile acids, disrupt the evacuation function of the gallbladder and contribute to the formation of bile sludge.

2. Old age: the cholesterol content in bile increases; metabolic processes and contractile function of the gallbladder decrease.

3. Heredity: genetic predisposition to the stone formation on the maternal and paternal lines and their combination, more often on the female line.

4. Metabolic disorders: obesity leads to increased synthesis and excretion of cholesterol, a low-calorie diet for weight loss is accompanied by the formation of putty-like bile and concretions, and bypass surgery for obesity increases the likelihood of cholelithiasis.

5. Physical inactivity.

6. Nutrition: violation of the diet and diet, eating a large amount of fatty, fried, spicy food, prolonged parenteral nutrition, fasting, rapid weight loss.

7. Long-term use of certain medications: contraceptives, hormonal drugs, antibiotics.

8. Some chronic diseases: diabetes mellitus, cirrhosis of the liver, Crohn's disease, helminthiasis, duodenal diverticula, and alcoholism.

9. In some cases, the onset of the disease can be triggered by injuries in the abdomen and spine [6,7].

The clinic of calculous cholecystitis is ambiguous and diverse. At an early stage, the disease may be asymptomatic. The severity of symptoms depends on the stage of development of the pathology and the individual characteristics of the patient. The first signs of a malfunction of the gallbladder are the appearance of the dyspeptic syndrome: dry mouth, white plaque on the tongue, nausea, sometimes vomiting (single or multiple, may be mixed with bile), belching, heartburn, a feeling of bitterness in the mouth or an unpleasant metallic taste, flatulence, stool disorders (diarrhea or diarrhea) [8-10].

The appearance of pain syndrome in the abdominal cavity is characteristic of the acute course of calculous cholecystitis [11,12]. Patients complain of severe pain in the right hypochondrium or back, of a pulling or aching nature, which can radiate into the back, under the right shoulder blade, into the left half of the trunk, and into the lower back. A third of patients complain of pain in the epigastric region. In some cases, there may be no characteristic localization of the pain syndrome.

The appearance of jaundice is a characteristic clinical syndrome in calculous cholecystitis. This symptom complex develops as a result of intoxication with bile acids and is manifested by the jaundice of the sclera, mucous membranes, and skin. Patients note severe itching of the skin, urine acquiring an uncharacteristic color, and feces discolors. The patient's condition is deteriorating. Further, intoxication syndrome develops, which is characterized by: general weakness, increased fatigue, syncopal states, headache, fever, and sleep disturbance [13-15].

2 Literature Review

Long-term scientific research has revealed a link between diseases of the gallbladder and bile ducts with diseases of the cardiovascular system. Therefore, a symptom complex was determined, characterized by a change in normal cardiac activity against the background of functional disorders of the gallbladder and biliary tract - cholecystocardial syndrome (biliary-cardiac syndrome, cholecystocoronary syndrome). This syndrome is characterized by the appearance of cardialgia (pain in the heart), rhythm and conduction disturbances due to metabolic disorders, sometimes deterioration of coronary circulation as a result of reflex, and infectious-toxic effects on the myocardium, due to damage by the pathological process of the gallbladder. In women, cholecystocoronary syndrome occurs 3 times more often than in men. The average age of patients is 35-55 years. Due to the variability of the manifestation of the condition, timely differential diagnosis and therapeutic measures are important [16-19].

The pathogenesis of cholecystocardial syndrome has several mechanisms of implementation: reflex effect on coronary vessels, metabolic disorders in the myocardium, and infectious and toxic effects on the cardiovascular system in the acute inflammatory process in the gallbladder and biliary tract. Afferent pathological impulses emanating from the extra- and intramural nerve plexuses of the bile ducts with spasm of the Lutkens, Mirizzi, Oddi sphincters and dilation of the bile ducts with biliary hypertension can affect the heart, through sympathetic and parasympathetic nerve fibers, causing spasm of coronary vessels and rhythm disturbances. With a

prolonged course of cholelithiasis with frequent attacks of biliary colic, complicated by chronic recurrent cholecystitis and concomitant disorders of the liver and pancreas, myocardial dystrophy develops, associated with complex disorders of the electrolyte, enzyme and carbohydrate balance, which can lead to disorders of the cardiovascular system. The ongoing inflammatory process in the biliary system has an infectious and toxic effect on the heart muscle, causing disturbances in the homeostasis system and the progression of myocardial dystrophy, causing increased excitability, conduction disorders and myocardial contractility [20-22].

Clinical manifestations of cholecystocardial syndrome have several variants. Cardialgic and angina-carditis forms are the most common manifestations: pain in the heart area of varying degrees and severity (acute, paroxysmal, compressive, stabbing) with irradiation to the right hypochondrium, from the right to the left hypochondrium with cholecystopancreatitis. With such a clinical picture, differential diagnosis with acute coronary syndrome is necessarily carried out. A pain-free form is also possible, accompanied by a violation of the heart rhythm: ectopic rhythm, extrasystole, atrial fibrillation, atrioventricular block, and blockage of the legs of the His bundle. Most authors believe that cardiac arrhythmia in the pathology of the biliary tract can be regarded as a manifestation of cholecystocoronary syndrome in cases of arrhythmia and the onset of biliary colic, the ineffectiveness of antiarrhythmic therapy, the transition of arrhythmia to a more severe form with the progression of inflammation in the biliary system. Often there is a simultaneous combination of pain and arrhythmia. Many clinicians with the pathology of the biliary tract note the appearance of symptoms such as tachycardia, increased pulse and venous pressure, occasionally revealing symptoms of hypertension in the small circle of blood circulation. In addition to subjective clinical manifestations, disturbances in the activity of the heart are also confirmed by objective changes in the ECG [23,24].

To diagnose cholelithiasis, a comprehensive study is prescribed: physical examination; laboratory examination of blood and urine; examination of the biliary system - ultrasound of the gallbladder and biliary tract, endoscopic retrograde cholangiopancreatography (magnetic resonance cholangiography and computed tomography are performed according to indications); examination of the cardiovascular system - ECG, Holter ECG monitoring (according to indications, tests with functional loads (bicycle ergometry, treadmill test), stress echocardiography, transesophageal electrical stimulation of the heart) are carried out. In the atypical course of cholelithiasis, differential diagnosis is performed between cholecystocardial syndrome and coronary artery disease, arrhythmias of another genesis, and acute coronary syndrome [25-27].

The results of the examination of patients with concomitant diseases of the cardiovascular system allow us to assess the functional tolerability of conservative and surgical treatment, to predict its results. Conservative treatment for calculous cholecystitis is carried out in the following cases:

- the presence of concretions in a bladder up to 10-15 mm in size with the preservation of its function and the patency of the cystic duct, filling the gallbladder with concretions no more than half;
- a serious condition of the patient before the improvement of the clinical picture;
- if it is impossible to remove bile cholesterol stones by surgical or endoscopic methods;
- patients who categorically refuse surgery.

Conservative treatment includes adherence to a strict diet with the restriction or complete exclusion of fatty, fried, spicy foods, and alcoholic and carbonated beverages. Prescribe a long-term intake (up to two years) of drugs that affect bile concretions, gradually dissolving them: ursodeoxycholic acid at 10 mg/kg, chenodeoxycholic acid at 15 mg/kg of body weight. With small sizes of concretions, noninvasive shock wave lithotripsy is performed [19,28].

In case of ineffectiveness of conservative therapy, the large size of concretions and unfavorable course of the disease, surgical treatment of calculous cholecystitis is used. Surgical interventions are open or laparoscopic removal of the gallbladder. In decompensation of the cardiovascular system, a two-stage treatment tactic is used: the first stage is simultaneous decompression and rehabilitation of the gallbladder (puncture or microcholecystostomy), the second stage is radical surgical intervention (after relief of acute inflammatory manifestations). With a combination of biliary hypertension and cholecystitis-cardiac syndrome, cardiac disorders in most cases are stopped only after the elimination of biliary hypertension, which is achieved with the use of endoscopic technologies and minimally invasive methods of bile removal (papillosphincterotomy, endoscopic lithotripsy, percutaneous microcholecystostomy, etc.) [29].

Modern studies have shown that the incidence of diseases of the biliary system and cardiovascular pathology are common conditions. Therefore, for a timely and correct diagnosis of cholelithiasis with manifestations of cholecystocardial syndrome, a specialist requires the ability to correctly collect a clinical history, conduct an optimal examination of the patient, analyze the results obtained and confirm the data obtained with the help of laboratory and instrumental studies. Complications developed as a result of diagnostic errors can lead to unfavorable and sometimes fatal outcomes. Depending on the cardiological manifestations and severity of diseases in the biliary system, the therapeutic tactics of the patient's management are determined. Timely relief of the pathology that has arisen contributes to a favorable prognosis.

This study examines the relationship of gender characteristics with cardiac manifestations of calculous cholecystitis.

3 Material and Methods

The study involved 80 patients with cholelithiasis (calculous cholecystitis) and cardiovascular pathology (CHD) aged 37-70 years. Patients with combined pathology were divided into two groups by gender: the first group - of 40 men (1), and the second group - of 40 women (2). Patients with only cardiac pathology were allocated to control groups of 40 men (1C) and women (2C).

The study was conducted in compliance with ethical principles and informed voluntary consent of patients. A comprehensive examination of the study participants included: a collection of complaints and anamnesis, physical examination, determination of body mass index (BMI), clinical blood test, and study of the coefficient of serum dyslipoproteidemia (CD) calculated according to the formula of A. N. Klimov. To confirm the cardiovascular pathology, ECG, Holter monitoring, echocardiography with color Doppler mapping of intracardial hemodynamics, and selective Judkins coronary angiography were performed [30-33]. Cholelithiasis was confirmed by clinical data and ultrasound of the abdominal organs.

Research methods used in the work include statistical, descriptive, comparative, and analytical. The obtained data were analyzed using Excel and Biostat statistical processing programs [34]. The data are presented in the form of averages with the determination of their errors ($\pm m$).

4 Results and Discussion

The study participants had certain clinical characteristics.

In the first group of patients (1), obesity was noted (BMI - 31.1); serum dyslipoproteidemia coefficient (CD) - 4.7; functional class III heart failure (FC III HF) - 40 people; painless myocardial ischemia (PMI) - 8 people; chronic heart failure (CHF) of the 1st degree of severity - 18 people and CHF of the 2nd degree of severity - 22 people; isolated, hemodynamically significant, stenosing lesion of various parts of the coronary artery - 30 people and multiple coronary artery stenoses - 10 people.

In the control group (1C), obesity was noted (BMI - 30.3); CD - 4.3; FC II HF - 8 patients and FC III HF - 32 patients; PMI - 6 patients; CHF of the 1st degree of severity - 32 patients and CHF of the 2nd degree of severity - 8 patients; isolated coronary artery stenosis - 6 patients and multiple coronary artery stenoses - 34 patients.

Table 1: Clinical characteristics of the study participants

Indicator	Study group			
	1	1C	2	2C
Age, years	64.5 \pm 5.0	55.0 \pm 4.8	58.3 \pm 6.8	60.4 \pm 3.4
Body Mass Index, kg/m ²	31.1 \pm 5.1	30.3 \pm 4.7	32.3 \pm 3.0	30.5 \pm 2.3
Coefficient of serum dyslipoproteidemia	4.7 \pm 1.6	4.3 \pm 0.8	4.9 \pm 1.8	3.7 \pm 1.3
functional class II heart failure, abs. (%)	40 (100.0)	8 (20.0)	4 (10.0)	28 (70.0)
functional class III heart failure, abs. (%)	-	32 (80.0)	36 (90.0)	12 (30.0)
painless myocardial ischemia, abs. (%)	8 (20.0)	6 (15.0)	18 (45.0)	8 (20.0)
chronic heart failure of the 1st degree of severity, abs. (%)	18 (45.0)	32 (80.0)	8 (20.0)	16 (40.0)
chronic heart failure of the 2nd degree of severity, abs. (%)	22 (55.0)	32 (80.0)	32 (80.0)	32 (80.0)
Isolated coronary artery stenosis, abs. (%)	30 (75.0)	22 (55.0)	6 (15.0)	22 (55.0)
Multiple coronary artery stenoses, abs. (%)	10 (25.0)	34 (85.0)	18 (45.0)	14 (35.0)

In the second group (2), obesity was noted (BMI - 32.3); CD - 4.9; FC II HF - 4 patients and FC III HF - 36 patients; PMI - 18 patients; CHF of the 1st degree of severity - 8 patients and CHF of the 2nd degree of severity - 32 patients; isolated coronary artery stenosis - 22 patients and multiple coronary artery stenoses - 18 patients.

In the control group (2C), obesity was noted (BMI - 30.5); CD - 3.7; FC II HF - 28 patients and FC III HF - 12 patients; PMI - 8 patients; CHF of the 1st degree of severity - 16 patients and CHF of the 2nd degree of severity - 24 patients; isolated coronary artery stenosis - 14 patients and multiple coronary artery stenoses - 26 patients.

Comparative data of the main and control groups are presented in Table 1.

The study data showed that patients with a combination of diseases of the biliary system and the cardiovascular system had more pronounced clinical cardiac manifestations, compared with patients with isolated cardiac pathology. Nevertheless, significant gender specificity was found in such patients.

In the study conducted in the control groups, the average age of women with coronary heart disease was older than that of men. This is probably due to the projective effect of estrogens during the reproductive period.

In the group of women with combined pathology, the average age was less than in women with isolated coronary artery disease, which may be due to the inadequate protective effect of estrogens. In women, against the background of metabolic disorders in the form of severe forms of obesity and dyslipidemia, gallstone disease can be a manifestation of lipid distress syndrome, in which prolonged excessive intake of exogenous cholesterol into the body disrupts the mechanism of lipid metabolism, contributing to the formation of gallstone disease. This, in turn, is considered a risk factor for the development of atherosclerotic lesions of the heart vessels, cerebral ischemia, coronary heart disease, arrhythmias.

The study also showed that women with cardiac pathology and cholelithiasis are more likely than men in a similar condition to have a painless form of myocardial ischemia, having an unfavorable prognosis of the course of the disease.

Isolated hemodynamically significant stenosis of one of the coronary arteries prevailed in both men and women. In the control groups, multiple coronary artery lesions were recorded, which contributed to the progression of CHF. The largest number of such patients were men.

Thus, the identified pathogenetic features and clinical manifestations of calculous cholecystitis and cardiac pathology are important for determining therapeutic measures.

5 Conclusion

In modern medicine, cases of combined pathology of the biliary system and the cardiovascular system are quite common. Since one of the clinical manifestations of cholelithiasis may be cholecystocardial syndrome, timely differential diagnosis of calculous cholecystitis with ischemic heart disease and acute coronary syndrome is of great prognostic importance at the stage of diagnosis of the disease.

In this study, the influence of gender characteristics on cardiac manifestations of calculous cholecystitis was studied. The results of the study showed that women with combined manifestations of diseases are at risk for an unfavorable course of cardiac pathology, and have a younger age of development of heart disease, and severe forms of obesity and dyslipidemia.

Calculous cholecystitis in men with cardiac pathology is a marker suggesting a long course of the disease and, as a consequence, the probable onset of depletion of the reserve capacity of the myocardium.

The information obtained is important in the prevention and treatment of diseases, thus contributing to a favorable prognosis.

6 Availability of Data and Material

Data can be made available by contacting the corresponding author.

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