

# МЕДИЦИНСКИЕ НАУКИ

## PREDICTION OF THE PROGRESSION OF CHOLELITHIASIS IN PATIENTS WITH PATHOLOGY OF THE HEPATOBILIARY SYSTEM

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### ABSTRACT.

**The aim of the study** is to predict the probability of the progression of cholelithiasis in patients with hepatobiliary diseases.

**Methods.** 396 patients aged 22 to 63 with different pathologies of the hepatobiliary system were examined. In verification of the diagnosis, along with anamnestic and general clinical data, were used the results of the ultrasonographic study of the biliary system. All patients underwent multifractional duodenal intubation, the total concentration of bile acids, cholesterol, phospholipids, and the cholato-cholesterol and phospholipid cholesterol coefficients. The level of anxiety was determined using a questionnaire developed by Charles Spielberg. The study of quality of life was performed using the questionnaire SF-36. The risk of cholelithiasis is calculated by formula. A screening questionnaire for predicting the probability of the progression of cholelithiasis was constructed using a logistic regression analysis method. The score prognostic table was compiled using a sequential diagnostic procedure, which is based on the method of sequential analysis.

**Results.** Abdominal pain and various symptoms of biliary dyspepsia were noted in 78% of patients. The most significant socio-hygienic factors in the progression of cholelithiasis are the alcohol abuse, non-compliance for the principles of rational nutrition, overweight or obesity, hypodynamia. The most important biomedical factors are attached to the presence of concomitant diseases of the gastrointestinal tract, the hereditary and hypersthenic type of constitution that is burdened by gallstones. The greatest pathogenetic significance in the progression of cholelithiasis as well as age, body mass index, number of pregnancies for women. The patient's gender, the contractile function of the gallbladder, the presence of concomitant chronic gastrointestinal diseases, dietary disorders, physical inactivity, stressful situations, harassment of heredity, smoking, alcohol abuse were taken into account among the dependent quality indicators.

**Conclusion.** The developed screening-questionnaire and the score prognostic table allow to identify patients at risk for the development of gastrointestinal disease.

The identified probability of the cholelithiasis development is the basis for an in-depth comprehensive examination of patients. The social effect of the introduction of the developed score prognostic tables will be determined by the improvement of the quality of life of patients, and the medical effect by the timely organization of prophylactic measures, taking into account the leading risk factors of cholelithiasis.

**Key words:** cholelithiasis, hepatobiliary system, anxiety, quality of life, gallstones risk factors, questionnaire.

### INTRODUCTION

Cholelithiasis is one of the urgent problems of clinical medicine due to the high insidens and much-accentuated negative influence on the quality of life [2, p.675;8,p.33].

The increase of surgery for cholelithiasis in recent years [6, p.34; 7, p.125] is largely because of the latent course of the disease [3, p.17; 4, p.36] and the diagnosis of cholelithiasis in the advanced stages, when conservative treatment methods are ineffective or they cannot be used. In this regard, there is a need for early diagnosis of cholelithiasis, as well as in the identification of patients at risk

for possible progression cholelithiasis.

The purpose of our study was to determine the prognostic criteria and evaluate their effectiveness in

identifying patients at risk for progression cholelithiasis.

### STUDIES AND RESEARCH METHODS

A focused and in-depth medical examination of 396 patients at the age of 22 to 63 years with various pathologies of the hepatobiliary system (functional disorders of the biliary system, chronic non-calculous cholecystitis, fatty hepatosis, chronic hepatitis of alimentary etiology) was held in the clinical conditions. The examination of the patients was carried out on the basis of the informed voluntary consent in accordance with ethical principles.

In verification of the diagnosis, along with anamnestic and general clinical data, were used the results of the ultrasonographic study of the biliary system. All patients underwent multifractional duodenal

intubation, the total concentration of bile acids, cholesterol, phospholipids, and the cholato-cholesterol coefficient (CCC) and phospholipid cholesterol coefficient (FLCC), which are indices of bile lithogenicity was determined in portions "B" and "C" [5, p.151]. Evaluation of lipid metabolism [1, p.67] was carried out on the content of total cholesterol in plasma, very low density lipoproteins, low density lipoproteins, high density lipoproteins, triglycerides (TG), with the calculation of atherogenicity (CA).

The level of anxiety was determined using a questionnaire developed by Charles Spielberg (USA) and adapted by Yu.L. Khanin, which allows the method of self-assessment to establish the level of reactive anxiety (RA) as current conditions and personal anxiety (PA) as sustainable human characteristics [9, p.66]. A questionnaire for the diagnosis of depressive states was developed for screening diagnostics during mass studies by William Tsung and adapted by T.I. Balashova.

The study of quality of life was performed using the questionnaire SF-36. For the quantitative determination of blood hormones (gastrin, insulin, cortisol), a competitive enzyme immunoassay was used.

The relative risk (RR) of anamnestic risk factors of cholelithiasis is calculated by this formula: the ratio  $a/n_1$  to  $b/n_2$ , where **a** is the frequency of occurrence of this factor among patients, **b** is the frequency of occurrence of this factor among persons in the control group, **n1** is the number of patients who have this

Table 1. Relative risk of gallstones risk factors

№	Name of risk factor	RR
<b>Biomedical</b>		
1	female gender	1,16
2	age over 45 years	1,94
3	burdened by cholelithiasis heredity	2,05
4	Hypersthenic type of constitution	2,15
5	Multiple pregnancies and (or) childbirth (more than 3)	1,62
6	Concomitant diseases of the gastrointestinal tract	6,37
<b>Socio-hygienic</b>		
7	alcohol abuse	6,25
8	Smoking	1,56
9	Non-compliance with the principles of good nutrition	3,6
10	Overweight or obesity	4,57
11	Hypodynamia	4,25
<b>Psychological</b>		
12	Frequent stressful situations, conflicts in the family and / or at work	1,81

So, as it turned out, the most significant socio-hygienic factors in the progression of cholelithiasis are the alcohol abuse, non-compliance for the principles of rational nutrition, overweight or obesity, hypodynamia. The most important biomedical factors in the progression of cholelithiasis are attached to the presence of concomitant diseases of the gastrointesti-

symptom, **n2** is the total number of patients. RR 1–2 was regarded as a moderate risk, RR 2,1–5 as a high risk, RR 5,1 and more as a very high risk.

A screening questionnaire for predicting the probability (P) of the progression of cholelithiasis was constructed using a logistic regression analysis method. The score prognostic table was compiled using a sequential diagnostic procedure, which is based on the method of sequential analysis.

The results of laboratory and instrumental studies were compared with data from the control group, which contained of 50 healthy individuals between the ages of 20 and 60 years.

## RESULTS AND DISCUSSION

Abdominal pain (mainly in the right hypochondrium) was noted in 78% of patients. The pain was more often constant, dull, aggravated when the body was tilted, accompanied by a feeling of pressure, distention with irradiation to the back, under the right shoulder blade, right shoulder or short-term, colic-like, arising after an error in the diet. In addition, the analysis of complaints revealed various symptoms of biliary dyspepsia (nausea, bitter taste in the mouth, heartburn, belching, constipation, or diarrhea).

The relative risk was estimated by all identified by history and general examination of the medical-biological, socio-hygienic, and psychological risk factors for cholelithiasis. (Table 1).

nal tract, the hereditary and hypersthenic type of constitution that is burdened by gallstones. All the risk factors identified by the anamnesis were taken into account.

during the compiling of the screening questionnaire to determine the likelihood of progression of cholelithiasis (Table 2),

Table 2. Screening questionnaire for patients with biliary symptoms

xn	Risk factors	points
x1	Gender male female	1 0
x2	Age less than 30 years from 30 to 49 years from 50 to 69 years over 70 years	1 2 3 4
x3	Heredity on cholelithiasis is burdened not burdened	1 0
x4	Body mass index less than 25 from 25 to 29 from 30 to 39 more than 40	1 2 3 4
x5	Constitution astenik normostenic hypersthenic	1 2 3
x6	Number of pregnancies (for women) no 1 or 2 3 or 4 5 or more	0 1 2 3
x7	Alcohol abuse yes no	1 0
x8	Smoking yes no	1 0
x9	Hypodynamy yes no	1 0
x10	Violation of he diet yes no	1 0
x11	Frequent stress yes no	1 0

Each accounted risk factor was assigned a sequence number (xn) and a corresponding score was assigned according to the formula:  $\ln P_{1-P} = b_1x_1 + b_2x_2 + \dots + b_nx_n$ , where  $x_1, \dots, x_n$  are independent signs (risk factors),  $b_1, b_2, \dots, b_n$  are regression coefficients,  $P_{1-P}$  is the odds ratio, that is, the ratio of the likelihood of progression of gallstones to the probability of their absence in the gallbladder. The significance of the regression equation was tested using the likelihood ratio criterion - 2LL.

Using the SPSS 13.0.1 package, the following logistic regression model was obtained:  $\ln P_{1-P} = z = 1,404x_1 + 2,085x_2 + 1,774x_3 + 2,397x_4 - 0,649x_5 - 0,227x_6 + 1,013x_7 - 1,668x_8 + 0,672x_9 + 2,102x_{10} + 0,102x_{11}$

$P = 11 + e^{-z}$ , where  $e$  is a constant (2,718).

As a result of testing the model, a probability separation point (P) was obtained equal to 0,7 (more than 0,7 - there is no probability of the progression of cholelithiasis, less than 0,7 - there is a probability of the progression of cholelithiasis). A sufficiently large sample shows the optimal specificity (82,0%), sensitivity (90,1%) and the percentage of correct classification (89,1%). The Nigelkerk coefficient of 0,836 suggests that the part of the variance explained by logistic regression is 83,6%. So, it is possible to consider that

the constructed model rather accurately predict the likelihood of the cholelithiasis progression only from clinical data.

The next stage of the prognostic search was the development of a prognostic score of the table (Table 3), which allowed to identify patients at risk for the progression of cholelithiasis on the basis of not only clinical but also laboratory and instrumental methods of research.

Independent and dependent quantitative and qualitative indicators analyzed were. From independent quantitative indicators, those laboratory and instrumental criteria were evaluated which have the greatest pathogenetic significance in the progression of cholelithiasis (bile lithogenicity indices and lipid metabolism indices affecting bile oversaturation with cholesterol, contractile function of the gall bladder, some neuro-hormonal regulation and mental status), as well as age, body mass index, number of pregnancies for women. The patient's gender, the contractile function of the gallbladder, the presence of concomitant chronic gastrointestinal diseases, dietary disorders, physical inactivity, stressful situations, harassment of heredity, smoking, alcohol abuse were taken into account among the dependent quality indicators.

Table 3. Prognostic table for identifying patients at risk for gallstones

	Categories	The presence or level of the studied characteristic	DC
1	CCC «B» (units)	<1,0	6
		1,0 - 3,0	4
		3,1 - 5,0	-8
		>5,0	-10
2	CCC «C» (unit)	<1,0	6
		1,0 - 3,0	4
		3,1 - 5,0	-8
		>5,0	-10
3	FLCC "B" (units)	<0,2	2
		0,2 - 0,4	-1
		>0,4	-3
4	FLCC "C" (units)	<0,05	2
		0,05 - 0,1	-1
		>0,1	-3
5	The contractile function of the gallbladder	normotonus	-12
		hypertonus	-9
		hypotonus	14
6	Chronic diseases of the gastrointestinal tract	no	-6
		there are	11
7	Diet disorder	no	-4
		there are	10
8	Cortisol (nmol / l)	<480,0	-10
		480,1 – 660,0	-4
		660,1 – 840,0	1
		>840,0	7
9	Triglycerides (g / l)	<0,3	-5
		0,3-1	-4
		1,1-1,7	1
		1,8-2,4	4
		>2,4	15
10	CA (units)	<1,1	-6
		1,1 – 3,0	-4
		3,1 – 5,0	1
		5,1-7,0	4
		>7,0	13
11	Smoking	no	-2
		yes	8
12	Stress	no	-2
		yes	8
13	Burdened by cholelithiasis heredity	no	-2
		there are	8
14	Hypodynamia	no	-2
		yes	8
15	RA (points)	<40	-5
		41-60	1
		>60	5
16	PA (points)	<40	-4
		41-60	2
		>60	5
17	Constitution	normostenik	-3
		astenik	-1
		hypersthenic	3
18	Alcohol abuse	no	-1
		yes	7
19	Insulin ( $\mu$ ed / ml)	<11,0	-3
		11,0 – 18,0	2

		>18,0	4
20	Body mass index (kg / m <sup>2</sup> )	<25,0	-2
		25,0 – 45,0	2
		>45,0	8
		<30,0	2
21	Gastrin (pg / ml)	30,0 и более	-2
		<60	-2
22	Depression (points)	60 и более	2
		<2	-3
23	Number of pregnancies	2	-1
		3	0
		4 и более	2
		<55	-1
24	Age	56-75	1
		>75	2

Indicators for the construction of a point scale were recoded into points (diagnostic factors - DC). With the sum of DC - 13 and less, the possibility of progression of cholelithiasis is extremely low. The amount of DC in the range from -12 to 12, means the average likelihood of risk of cholelithiasis; the sum of DC 13 and more - means a high risk of progression of cholelithiasis.

The sensitivity of the developed model is 98,02%, specificity is 98,00%.

#### FINDINGS

1. The developed screening-questionnaire and the score prognostic table allow to identify patients at risk for the development of gastrointestinal disease.  
3. The identified probability of the cholelithiasis development ( $P < 0,7$ ) is the basis for an in-depth comprehensive examination of patients.  
4. The social effect of the introduction of the developed score prognostic tables will be determined by the improvement of the quality of life of patients, and the medical effect by the timely organization of prophylactic measures, taking into account the leading risk factors of cholelithiasis.

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