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MANODEBITOMETRY OF EXTRAHEPATIC CHOLESTASIS IN COMPLICATED CHOLELITHIASIS

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Introduction.

Temporary or prolonged extrahepatic cholestasis (EHC), according to many authors, is one of the main etiological factors in the development of cholelithiasis (CL), as one of the most common digestive disease [1-4]. At the same time, if the patient does not have a clinical picture of EHC, the diagnosis sounds like CL, chronic cholecystitis, such patients often perform laparoscopic cholecystectomy (LCE), during which the exploration of bile duct for EHC and the reasons, that it caused, is not performed. Complications that develop after LCE (postcholecystectomy syndrome, mechanical jaundice, chronic pancreatitis, etc.) are frequent causes of diagnostic errors in the subsequent treatment of this group of patients. Despite the development of medical equipment, improvement of surgical skills and many scientific publications, there are many unresolved issues of intraoperative diagnosis of EHC in CL in this group of patients. Introduction into clinical practice of ultrasound, MRCP, ERCP, EUS allow in the vast majority of cases before surgery to establish the cause of bile passage in patients with CL in the preoperative period, perform decompression of the biliary tract during surgery, and then either eliminate the cause of bile passage violation with minimally invasive interventions, or prepare the patient for the next stage of surgical treatment [4-9]. However, it is not always possible before and during surgery to determine the cause of EHC in CL using modern diagnostic methods.

At the same time, determining the degree of biliary hypertension is undoubtedly important for the physician, because in the decompensation of bile outflow the bile hypertension leads to functional and then pathomorphological changes in the hepatobiliary system, which causes a number of complications. Thus, the head of the group of experts involved in the preparation of criteria for functional disorders of the gallbladder (GB) and sphincter of Oddi (SO) E. Corazziari in 1999 was forced to admit: "We often can’t distinguish between functional disorders of the

biliary tract and hidden organic changes. This is due to the peculiarities of the anatomical location of the GB, the imperfection of the research methods used now, and the lack of uniform histological criteria in the assessment of minimal structural changes in the biliary tract "[2]. And even with fully compensated bile outflow, persistent and long-standing biliary hypertension also causes a number of pathological changes in the biliary tract and liver, causing the transition of dyskinesia of SO to stenosis, especially in the presence of stones or sludge in the common bile duct [1-6,10 , 11].

The method of cholangiomanometry, proposed in 1868 by Heidenhain, has undergone many modifications over the past century. V.Vinogradov, E.Grishkevich, Mallet-Guy, Lardi, Hessi, Lehner, Roux believed that no bile duct surgery should be done without manometry, and its main purpose- to identify the causes of functional and organic obstructions in the biliary system that disrupt bile flow-remains. [10-12].

Therefore, manometry, used in biliary surgery since the mid-nineteenth century and to this day, is the "gold standard" in the diagnosis of functional disorders of the sphincter apparatus of the biliary system, and the efficiency of method is 92 - 97% [2-4,8].

In 1952, Cannuel, Debray, and Roux Petit proposed that a certain amount of fluid should be passed through the common bile duct over a constant period of time. This method is called debitometry. A number of researchers [11,12] note the great simplicity of this method as an advantage over manometry and more accurate reflection of hydrodynamic changes in pathological conditions of the biliary tract, so the combination of both methods is predicted to increase the possibility of intraoperative diagnosis of functional and organic pathology of the biliary tract. with modern methods of visualization of the duct system.

However, to date, the effectiveness of the combined method of manodebitometry in the intraoperative diagnosis of the main causes of EHC in CL has not been established. **So, the purpose of our study was** to evaluate the effectiveness of the combined method of manodebitometry in intraoperative diagnosis of the causes of different types of extrahepatic cholestasis in complicated cholelithiasis.

Materials and methods.

The manodebitometry was performed in 181 patients who were operated in the Department of Digestive Surgery of the State Institution «Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine» for the period from 2013 to 2020. Indications for surgical treatment were: chronic calculous cholecystitis - in 59 (32.59%); chronic calculous cholecystitis with choledocholithiasis - in 64 (35.35%); choledocholithiasis after cholecystectomy - in 18 (9.94%); postcholecystectomy syndrome with stenotic papillitis - in 40 patients (22.09%).

Patients with the following comorbidities were excluded from the study: viral and autoimmune hepatitis; Carolli's disease; Wilson-Konovalov disease; Gilbert's syndrome; oncological genesis of jaundice, metabolic syndrome.

The age of the examined patients ranged from 27 to 83 years, on average (58.23 ± 1.69) years. The largest number of patients were patients aged 40 to 69 years. There were 52 men (28.73%) and 129 women (71.27%).

To perform the manodebitometry we have developed a software and hardware complex consisting of a certified digital domestic manometer MNH-01 ALAN 941118.001, which through a switching cable connected to the invasive pressure sensor UTAH DPT-248A in one side, and in the other side through a 10-centimeter connector, that excludes wetting of the sensor, to the three-way valve. A 100 ml Jeanne syringe, which serves as a measuring container with a polymer tube with liquid flow regulator from a standard system for intravenous infusion through a compensatory vent cistern, is connected to the second port of the three-way valve. An extension cord is connected to the third port of the valve, which connects to the bile duct catheter. Pressure recording is performed on a tablet computer monitor using the ALAN software package. Data is exchanged between the digital manometer and the computer via a USB port.

The principle of the device is based on converting the displacement of the membrane under the influence of the column of fluid filling the catheter into an electrical signal, which is amplified and digitally converted to a computer, where it is processed numerically, graphically visualized and stored in *. dat format. After

cannulation of the choledochus through the GB duct with a drainage tube or retrograde catheter during ERCP, the drainage cannula or catheter in ERCP is connected to an invasive pressure transducer. The sensor is installed at the level of the medium axillary line in the right hypochondrium, which anatomically corresponds to the level of the large duodenal papilla (LDP) and through a three-way valve connects to a system containing a compensatory vent cistern with a clearly marked fluid level filled with sterile, heated to 37 ºC isotonic 0.9% NaCl solution or X-ray contrast solution (Figure 1)

Fig.1. Device for performing intraoperative manodebitometry

The manodebitometry is a very sensitive method of research, its performance depends on many reasons. The local trauma in the area of GB, the common bile duct and in the area of LDP has a special influence. Careful palpation has little effect on these parameters, but the allocation of GB, especially the vesical and common bile ducts, is accompanied by the dissection of numerous branches of the hepatic nerve plexus. This leads to a temporary decrease the SO tonus, a partial decrease in residual pressure and an increase of fluid debit. Probing or intraductal exploration of the common bile duct and LDP can lead to local edema, spasm of the sphincter, increased residual pressure and decreased debit. Therefore, if the performing of manodebitometry planed, it is necessary that the injury be as minimal as possible.

To increase the specificity of radiological methods of bile duct visualization [8, 10, 11] and, most importantly, differential diagnosis of the causes of functional and organic SO disorders, we performed intraoperative administration of papillorelaxants (in particular, nitrates or M-cholinolytics), which promote relaxation of SO. In the

absence of a passage of contrast agent through SO, we performed a SO "relaxation test" - administered intravenously bolus 10-20 mg (1-2 ml.) of isosorbide dinitrate or 20 mg of hyoscine butylbromide, and then after 2 minutes the study was repeated.

Thus, the SO "relaxation test" was considered positive in restoring the passage of contrast fluid after the introduction of papillorelaxants, and negative if it did not. Due to non-specificity of symptoms, when they are detected in the first place should be excluded neoplasms of the pancreatobiliary zone and choledocholithiasis.

After filling the system, the compensating cistern and the choledochus, the initial pressure parameters in the duct were registered. The pressure required for manodebitometry was created by further increasing the liquid column until the pressure values were fixed on a digital manometer with a fixed set level of 300 mm of water column (mm H2O) and with the advent of relative isoline on a portable tablet computer, after which the manodebitometric camera was fixed on a tripod. Then we performed registration of pressure and debit in accordance with physiological norms according to V. Vinogradov (1964) [11].

The concentration of total bilirubin in the serum was determined according to the instructions to the kits of EliTech (France). The activity of alanine-aminotransferase (ALT), aspartate-aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyltransferase (GGT) serum was determined by ultraviolet kinetics (ALT/GPT, AST - AST/GOT), recommended by the International Federation of Clinical Chemistry (IFCC) according to the instructions of the EliTech kits (France).

The presence of endogenous intoxication (EI) was determined by the content of medium molecular weight peptides (MMP) according to V.V. Nikolaychuk. The MMP fraction consists of aromatic amino acids, which are part of proteins, collagen fibers, aromatic amino acids, among which tyrosine and tryptophan occupy a significant place, and therefore the increase in the content of MMP in serum is a marker of activation of catabolic processes in the body.

Fibrosis processes were evaluated by the content of hydroxyproline free (HPf) and glycosaminoglycans (GAG). In serum, the content of GAG was determined according to Rimington, HPf - by Osadchuk, the activation of the inflammatory process in patients was evidenced by a change in the level of alpha-1-acid

glycoprotein, the content of which was determined by Weimer [16]. Assessment of biochemical parameters was given according to their content in blood of relatively healthy 20 persons (control group).

The ultrasound investigation was performed in all patients, and on suspicion of choledocalculosis were performed ERCP which was carried out in 79 (43.64%) patients as diagnostics and treatment manipulation and MRCP performed in 58 (32.04%) patients.

For the assessment of the motoric and evacuation function of the GB (MEF GB) before the operation in 52 (28.72%) patients which have no contraindication, such as small stones or inhomogeneous content of GB or choledohus in ultrasound investigation, using following method: the initial volume (V1) of GB was determined on an empty stomach, then after a trial cholekinetic breakfast (20 g of sorbitol dissolved in 50 ml of warm water) the volume of GB was determined per minute for the first 10 min and then every 10 min until the GB was relaxed. The volume of GB after its maximum contraction (V2) was used to determine the efficiency of bile secretion (EBS):

$$\text{EBS} = \frac{V1 - V2}{V1} * 100\%$$

The EBS of GB was considered normal if in 20-40 minutes after a cholekinetic breakfast, the maximum EBS was 40 - 70% of the initial volume of GB. Assessment of the functional state of the GB was performed taking into account the primary reaction, latency period, and a time of maximum contraction of the GB [13].

During the operation, all patients underwent manodebitometry, the indicators of which were compared with the data of X-ray cholangioscopy and -graphy. The main time for manodebitometry was occupied by the process of cannulation of the vesical duct, and in fact, the study time, depending on the need for repeated measurements, took an average of (7.2 ± 3.6) minutes.

The research was performed in compliance with the "Rules of ethical principles of scientific medical research with human participation", approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EEU Directive № 609 (dated 24.11.1986), orders Ministry of Health of Ukraine № 690 dated 23.09.2009, № 944 dated 14.12.2009, № 616 dated 03.08.2012 Each patient signed an informed

agreement to participate in the study, taking all measures to ensure the anonymity of patients.

Statistical analysis of the obtained data was performed using Excel applications Microsoft Office 2010 and Statistica 12.0. The median (Me), lower and upper quartiles (Q25; Q75) were used to describe the data. The comparisons were performed using a nonparametric criterion (U-test Mana-Whitney).Comparison of mean values was performed using Student's t-test. The difference was considered significant if the achieved significance level (p) was less than 0.05. To assess the diagnostic effectiveness of the indicators used ROC analysis to determine the area under the ROC curve (AUC), the optimal threshold value, sensitivity and specificity.

Results and discussion. In 30 patients diagnosed with "chronic calculous cholecystitis" in the preoperative period according to biochemical studies of blood markers of cholestasis were not detected (control group), but in anamnesis of these patients were indirect clinical signs of EHC: episodes of scleral yellowing, darkening of urine, had a history of predictors of EHC, namely: pregnancy, oral contraceptives or other hormonal drugs intake, diabetes, episodes of prolonged starvation or parenteral nutrition, truncal vagotomy, therefore, this cohort of patients was allocated to a separate "temporary" type 0 of EHC (with anamnestic episodes of extrahepatic cholestasis).

Among 151 patients by the severity of biochemical markers of cholestasis, 4 types of EHC were identified:

The type I of EHC - without jaundice and without damage to hepatocytes (n = 50) - the average level of bilirubin was 23.5 ± 1.7 μmol \ l, ALT - 38.2 ± 3.45IU / l, AST - 36.9 ± 4 , 14 U / l, which indicated the absence of cytolysis, and AF - 284 ± 32.4 U / l and GGTP - 247 ± 34.6 U / l - the presence of EHC, the level of MMP-726 ± 36 g / l;

The type II of EHC - without jaundice with hepatocyte damage (n = 38) - the average level of bilirubin was 34.7 ± 3.2 μmol \ l, ALT - 136 ± 27.8IU / l, AST - 84.13 ± 15.5 U / l, which indicated the presence of cytolysis, and indicators of AF - 262 ± 32.8IU / l and GGTP - 345 ± 37.6IU / l - the presence of EHC, the level of MMP - 902 ± 56.4g / l;

The type III of EHC - with jaundice without damage to hepatocytes (n = 36) - the average level of bilirubin was 159 ± 12.75 μmol \ l, ALT - 39.8 ± 5.1 / l, AST - 40.4 ± 6.8 U / l, which indicated the presence of cytolysis, and indicators of AF - 310 ± 59.1IU / l and GGTP - 260 ± 41.4IU / l - the presence of EHC, the level of MMP - 1050 ± 75.7 g / l;

The type IV of EHC - with jaundice and hepatocyte damage (n = 27) - the average level of bilirubin was 313.8 ± 28.1 μmol \ l, ALT - 287 ± 44.6IU / l, AST - 242 ± 49.67 U / l, which indicated the presence of cytolysis, and indicators of AF - 630 ± 81.2IU / l and GGTP - 610 ± 69.9IU / l - the presence of EHC, the level of MMP - 1139 ± 78.4 g / l.

Indicators of the cause of EHC in complicated CL, which were established before surgery and clarified during surgery by radiological studies, were compared with the indicators of manodebitometry (Table 1).

Table 1. Manodebitometric parameters of the established causes of different types of EHC in complicated CL

Types of EHC	Established cause of EHC	Pressure in the choledoch, mm H20 Me (Q_{25} ; Q_{75})		Debit, ml / min Me (Q_{25} ; Q_{75})		Coefficient Me (Q_{25} ; Q_{75})
		initial	final	initial	final	
Type 0 of EHC	Chronic calculous cholecystitis, n=21	96,3 (71,8 ; 119,5	48,2 (42,6 ; 60,4)	19,3 (11,1 ; 27,5)	37,9 (28,8 ; 44,4)	2,51 (2,35 ; 2,60)
	Sphinter of Oddi dysfunction (SOD), n=6	130,3* (112,7 ; 144,2)	97,1* (83,4 ; 110,8)	7,4* (6,6 ; 9,2)	23,9* (19,4 ; 26,4)	1,65* (1,54 ; 1,76)
	SOD + stenotic papillitis 0-1 st., n=3	144,4* (142,6 ; 151,7)	119,6* (99,5 ; 136,4)	9,5* (8,8 ; 10,8)	21,1* (20,3 ; 24,6)	1,66** (1,58 ; 1,72)
Type I of EHC	SOD + stenotic papillitis 0-1 st., n=22	135,2* (115,5 ; 153,1)	115,9* (104,6 ; 131,4)	11,3* # (9,7 ; 22,5)	22,2* (18,4 ; 30,4)	1,66* (1,53 ; 1,77)
	Floating calculus, n=15	132,5* (117,2 ; 151,6)	191,3* # ^ (174,9 ; 223,3)	19,7 # ^ & (12,1 ; 31,1)	5,5* # ^ & (5,1 ; 7,4)	4,27* # (3,84 ; 4,73)
	Stenotic papillitis 1 st., n=13	144,6* (128,3 ; 159,9)	180,8* # ^ (154,6 ; 200,7)	10,1* # (7,2 ; 16,7)	8,9* # ^ (6,1 ; 12,4)	1,93* # (1,80 ; 2,00)
Type II of EHC	Stenotic papillitis 1-2 st., n=11	188,7* # (168,6 ; 201,9)	191,4*# ^ (175,5 ; 214,4)	7,9* (7,2 ; 8,6)	8,0* # ^ (7,4 ; 8,7)	1,97* # (1,89 ; 2,02)

	Floating calculus with stenotic papillitis 1-2 st., n=15	194,8* # ^ (183,2 ; 214,4)	210,1* # ^ (199,1 ; 229,7)	16,5 # & (13,3 ; 20,4)	6,5* # ^ (4,8 ; 9,9)	3,47* # & (3,27 ; 3,61)
	Floating calculus, n=12	137,9* & ° (117,6 ; 160,4)	215,3* # ^ & (192,4 ; 243,7)	21,6# ^ & ° (16,5 ; 30,1)	5,1* # ^ (4,0 ; 8,8)	4,88* # & ° (4,56 ; 5,13)
Type III of EHC	**Stenotic papillitis 2 st., n=5**	230,5* # ^ (216,1 ; 244,5)	242,8* # ^ (228,3 ; 260,8)	6,6* (6,6 ; 7,0)	6,5* # ^ (6,2 ; 6,8)	1,96* # (1,84 ; 2,03)
	Floating calculus, n=13	166,4* & (142,9 ; 187,1)	240,9* # ^ (204,5 ; 258,8)	19,7# ^ & (16,6 ; 21,4)	5,5* # ^ (4,6 ; 7,2)	4,27* # & (3,72 ; 4,68)
	Floating calculus with stenotic papillitis 2 st., n=7	242,7* # ^ (224,1 ; 261,1)	280,2* # ^ & (262,6 ; 303,7)	13,9* # & (12,8 ; 14,7)	5,0* # ^ (4,1 ; 5,9)	3,65* # & (3,42 ; 3,71)
	Wedged calculus, n=11	272,2* # ^ & (253,6 ; 287,1)	294,7* # ^ & (273,3 ; 311,4)	5,0* # ^ & ° (4,8 ; 5,3)	1,0* # ^ & ° (1,0 ; 1,5)	5,92* # & ° (5,81 ; 6,04)
Type IV of EHC	**Stenotic papillitis 3 st., n=4**	301,4* # ^ (284,2 ; 318,4)	311,9* # ^ (295,1 ; 327,6)	5,5* # ^ (5,3 ; 5,8)	5,4* # ^ (5,2 ; 5,6)	1,98* # (1,92 ; 2,03)
	Floating calculus with stenotic papillitis 3 st., n=3	291,1* # ^ (270,0 ; 305,5)	308,9* # ^ (288,1 ; 321,4)	5,6* ^ (4,9 ; 6,2)	2,7* # ^ & (2,3 ; 3,1)	3,02* # & (2,95 ; 3,12)
	Wedged calculus, n=13	298,3* # ^ (284,4 ; 311,4)	304,6* # ^ (290,2 ; 315,1)	4,9* # ^ (4,6 ; 5,5)	1,0* # ^ & ° (1,0 ; 1,4)	5,88* # & ° (5,72 ; 5,99)
	Biliary fistula (Mirizzi's syndrome), n=7	Variable data, the diagnosis is established intraoperatively and radiographically				

Notes:

1. * - p <0,05– significance of the difference of indicators in relation to the group of patients with chronic calculous cholecystitis;

2. # - p <0,05 - the significance of the difference in indicators relative to the group of patients with DSO;

3. ^ - p <0,05 - the significance of the difference between the group of patients with DSO + stenotic papillitis;

4. & - p <0,05 - the significance of the difference between the group of patients with stenotic papillitis within one type of PCS;

5. ° - p <0.05; - the significance of the difference between the group of patients with floating stones with stenotic papillitis within one type of PCS.

Comparison of manodebitometry data with the indicators of the causes of EHC in complicated CL, established on ultrasound data before surgery and refined radiologically during the operation, allowed to determine that in the form of **manodebitometric coefficient** parameters of the main causes of each type of EHC statistically differ in the types and reflecting the staged development of EHC in complications of CL.

Discussion.

Preoperatively undiagnosed phenomena of isolated stenotic papillitis at different stages of formation were detected intraoperatively using manodebitometry with radiological verification in 34 (18.78%) patients, including:

- 13 (7.18%) patients with type I of EHC;

- 19 (10.49%) patients with type II of EHC (including 7 (3.86%) patients in combination with choledocholithiasis);

- 8 (4.41%) patients with type III of EHC (including 3 (1.65%) patients in combination with choledocholithiasis;

- 7 (3.86%) patients with type IV of EHC, of which 3 (1.65%) patients in combination with choledocholithiasis.

The combination of choledocholithiasis of stenotic papillitis was found in 13 (7.18%) patients.

Isolated SO dyskinesia as functional disorders due to LCE in the anamnesis were found in 6 (3.31%) patients with type 0 of EHC and in 7 patients (3.86%) with type III of EHC.

In 25 (including 3 (1.65%) patients with type 0 of EHC and in 22 (12.15%) patients with type II of EHC, the phenomena of SO dysfunction were determined in combination with structural disorders at the stage of formation (SO dyskinesia + stenotic papillitis at the stage of formation, 0-1st.).

It should be noted that patients with type 0 of EHC at the time of surgery did not have any biochemical predictors of cholestasis.

The diagnosed stage of stenotic papillitis formation corresponded to a certain type of EHC, however, according to the results of studies in 11 patients with type II of EHC (6.07% of the total and 28.94% of patients with type II of EHC) the

phenomena of stenotic papillitis, manometric parameters which does not clearly correspond to the existing classification (V. Vinogradov, E. Grishkevich, 1963), so this cases were defined as a stenosis of SO of I-II st.

Due to the certain variability of the parameters of the residual pressure of choledochus and fluid debit at the beginning of the study and after the injection of papillorelaxants (nitrates, M-cholinolytics) at the end of the study – we decided to obtain an integral numerical coefficient :

$$\text{Debit (D)} = \frac{D\ initial}{D\ final}$$

$$\text{Pressure (P)} = \frac{P\ \ initial}{P\ \ final}$$

Manodebitometric coefficient (C) = Debit (D)) + Pressure (P)

For example, for patients with type 0 of EHC in whom SO dysfunction was detected, the initial pressure and debit were 140.6 mm H_2O and 7.4 ml / min, final pressure - 108 mm H_2O and 27 ml / min, respectively (against the background of the introduction of papillorelaxants after the first minute of the study, see Fig. 2), respectively, T = 1.3 (140.6 / 108), and D = 0.27 (7.4 / 27) , respectively C = 1.57 (1.3 + 0.27).

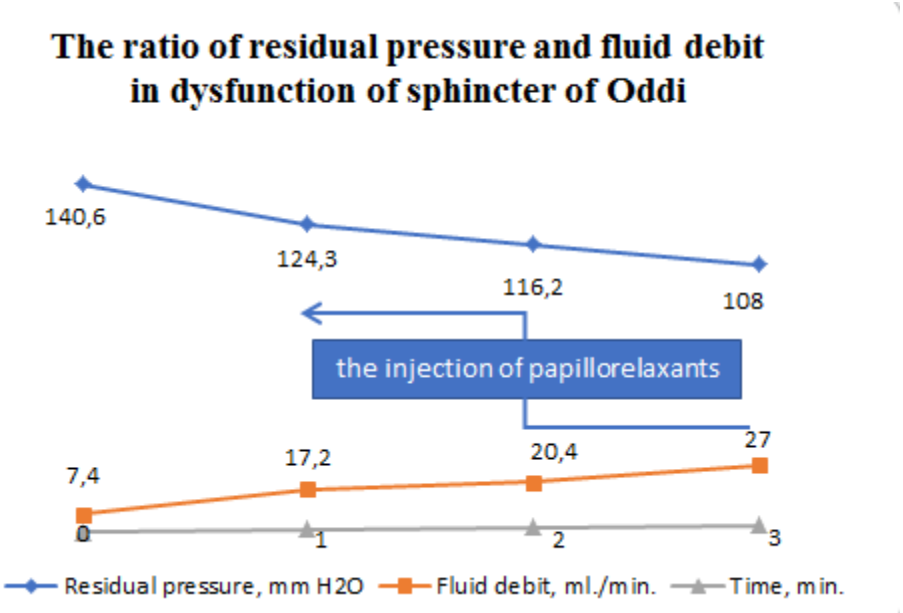

Fig. 2. An example of the detected ratio of flow and pressure parameters in dysfunction of the sphincter of Oddi

According to the ratio of the sum of the values of the pressure fraction at the beginning and end of the study and the fraction of fluid debit during one minute and

at the end of the study (before and after the relaxation test), the following coefficients can be distinguished for intraoperative pathology screening (Fig. 3).

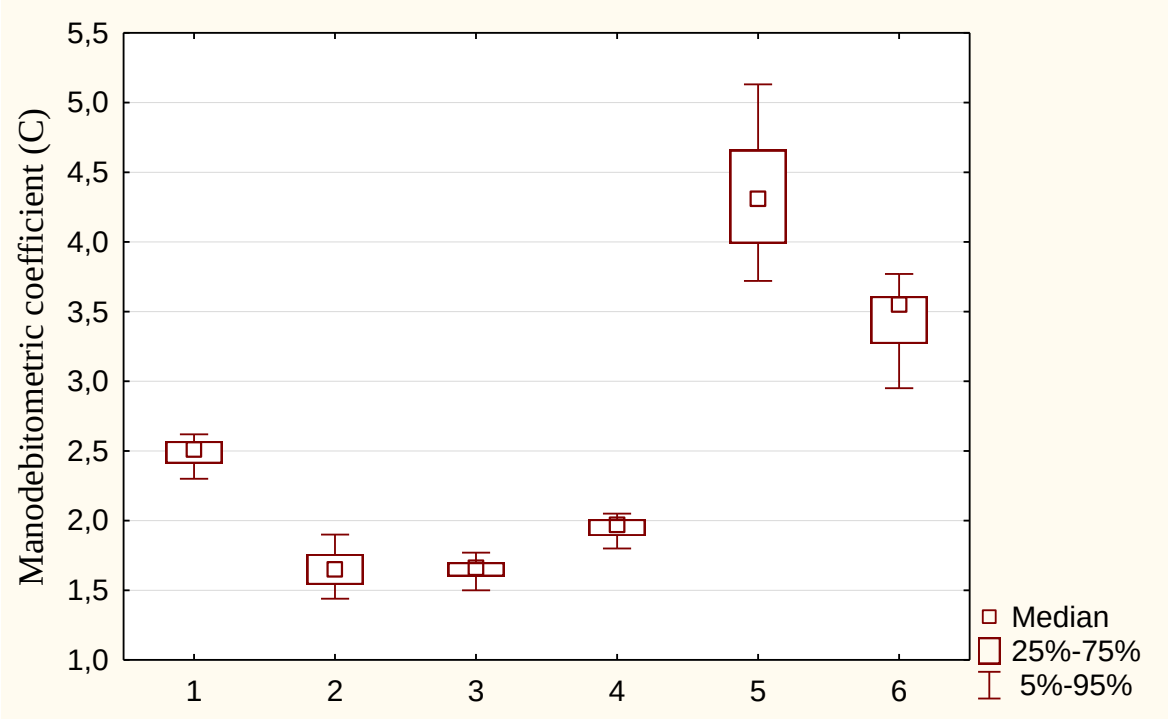

Fig.3. Distribution of manodebitometric coefficient at different causes of EHC in complicated CL

Notes:

1 - Chronic calculous cholecystitis, uncomplicated;
2 - Sphinter of Oddi dysfunction (SOD);
3 - SOD + stenotic papillitis;
4 - stenotic papillitis;
5 - Floating calculus;
6 - Floating calculus with stenotic papillitis

Therefore, as can be seen from the distribution, the determined coefficient for different causes of cholestasis for organic disorders of SO will always be in the parameters of 1.8-2.03, and in functional disorders - always lower than 1.8. The coefficient of uncomplicated chronic calculous cholecystitis is in the range of 2.35-2.6, and an index above 2.6 allows us to suspect the presence of floating stones.

Thus, the use of a combined method of manodebitometry in the intraoperative diagnosis of the main causes of different types of EHC in complicated CL, allowed in 34 (18.78%) patients to diagnose organic disorders as the cause of EHC and in 38 (20.99%) patients - functional violation of the sphincter apparatus. The number of

intraoperatively detected structural and functional disorders is 39.77% among operated patients.

When conducting ROC-analysis, the use of a combined method of manodebitometry as a diagnostic screening of functional and organic causes of EHC in complicated CL allowed to establish a high quality diagnostic model using a factor of 1.6 as the optimal classification threshold (Fig. 4) with an accuracy of 88.9 %, sensitivity 93, 6%, specificity 80%, as AUC = 0,9311 (95% CI 0,918-0,929; p <0,0001).

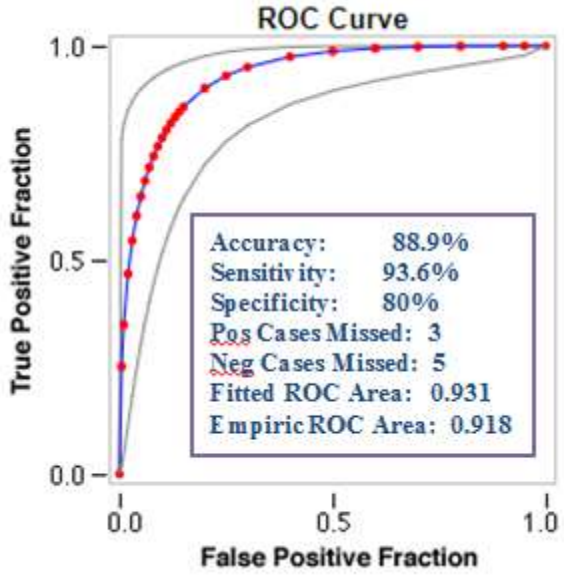

Fig.4. ROC-curve of the integral coefficient as a diagnostic criterion for identifying the structural or functional cause of EHC in CL

Therefore, the analysis of the results of the evaluation of the use of the combined method of manodebitometry in the examined patients showed high sensitivity and specificity of the obtained data in the established both organic and functional genesis of EHC in complicated CL.

CONCLUSIONS:

1. The combined method of manodebitometry, which consists in determining of pressure in the extrahepatic bile ducts and the debit of perfused fluid through the terminal part of choledochus per unit time, allows to increase up to 34.8% the detection of EHC in complicated CL and establish it functional and organic causes during surgery.

2. Due to its simplicity, easy reproducibility and diagnostic value (accuracy 88.9%, sensitivity 93.6%, specificity 80%), manodebitometric study according to the developed method can be recommended for practical application for the recognition of EHC type in complicated CL, its main causes and intraoperative determination of indications for their correction during surgery.

3. The use of manodebitometric examination of the choledochus with a pharmacological test for relaxation, allows to make a clear idea of the functional state of the muscular apparatus of the sphincter of Oddi and to detect its dysfunction.

4. Manodebitometry is considered necessary in all doubtful cases, which can significantly reduce the number of undiagnosed causes of EHC in complicated CL and, in the long run, the development of postoperative complications.

Conflict of interest. The authors declare the absence of conflict of interest and their own financial interest in the preparation of this article.

Key words: manodebitometry, extrahepatic cholestasis, complicated cholelithiasis

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МАНОДЕБІТОМЕТРІЯ ПОЗАПЕЧІНКОВОГО ХОЛЕСТАЗУ ПРИ УСКЛАДНЕННОМУ ХОЛЕЛІТІАЗІ

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Мета роботи: оцінити ефективність застосування об'єднаної методики манодебітометрії в інтраопераційній діагностиці причин різних типів позапечінкового холестазу при ускладненому холелітіазі.

Матеріали і методи досліджень. Манодебітометрія проведена у 181 хворого, які були оперовані у відділенні хірургії органів травлення ДУ "Інститут гастроентерології НАМН України" за період з 2013 по 2020 рр..за допомогою розробленого апаратно-програмного комплексу. Всім хворим до операції виконували: УЗД, а при підозрі на холедохокалькульоз - РХПГ та МРХПГ. Також оцінювалась моторно-евакуаторна функція жовчного мухіра.

Результати та обговорення. В залежності від наявності біохімічних маркерів жовтяниці та пошкодження гепатоцитів, а також наявності предикторів холестазу в анамнезі, хворі були розподіленні на 5 груп поза печінкового холестазу (ПХС).

Застосування об'єднаної методики манодебітометрії в інтраопераційній діагностиці головних причин різних типів ПХС при ускладненому холелітіазі

(ХЛ), дозволила у 34 (18,78%) хворих діагностувати органічне порушення як причину розвитку ПХС, та у 38 (20,99%) - функціональні порушення сфінктерного апарату ВДС. Проведення ROC-аналізу застосування об'єднаної методики манодебітометрії в якості діагностичного скринінгу функціональної та органічної причин ПХС при ускладненому ХЛ дозволило встановити високу якість діагностичної моделі з використанням визначеного коефіцієнту в якості оптимального порогу класифікації з точністю 88,9%, чутливістю 93, 6%, специфічністю 80%, так як AUC=0,9311 (95 % ДІ 0,918-0,929; p<0,0001).

Висновки. Застосування манодебітометрічного дослідження холедоха з фармакологічним тестом на розслаблення дозволяє під час операції на 34,8% збільшити виявлення причин ПХС при ускладненому ХЛ, виявити його дисфункцію і може бути рекомендовано до практичного застосування для розпізнавання типу ПХС при ускладненому ХЛ, його головних причин та інтраопераційного визначення показань для їх корекції під час операції.

МАНОДЕБИТОМЕТРИЯ ВНЕПЕЧЕНОЧНОГО ХОЛЕСТАЗА ПРИ ОСЛОЖНЕННОМ ХОЛЕЛИТИАЗЕ

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Цель работы: оценить эффективность применения объединенной методики манодебитометрии в интраоперационной диагностике причин различных типов внепеченочного холестаза при осложненном холелитиазе.

Материалы и методы исследований. Манодебитометрия проведена у 181 больного, которые были прооперированы в отделении хирургии органов пищеварения ГУ "Институт гастроэнтерологии НАМН Украины" за период с 2013 по 2020 гг с помощью разработанного программно-аппаратного комплекса. Всем больным до операции выполняли: УЗИ, при подозрении на холедохокалькулез − ЭРХПГ и МРХПГ, проводилась диагностика моторно-эвакуаторной функции желчного пузыря.

Результаты и обсуждение. В зависимости от наличия биохимических маркеров желтухи и повреждения гепатоцитов, а также наличия предикторов

холестаза в анамнезе, больные распределены на 5 групп внепеченочного холестаза (ВХС).

Применение объединенной методики манодебитометрии в интраоперационной диагностике главных причин различных типов ВХС при осложненном холелитиазе, позволила у 34 (18,78%) больных диагностировать органическое нарушение как причину развития ВХС, и у 38 (20,99%) пациентов − функциональные нарушения сфинктерного аппарата БДС. Проведение ROC-анализа применения объединенной методики манодебитометрии в качестве диагностического скрининга функциональной и органической причины ВХС при осложнениях ХЛ позволило установить высокое качество диагностической модели с использованием определенного коэффициента в качестве оптимального порога классификации с точностью 88,9%, чувствительностью 93,6%, специфичностью 80%, AUC = 0,9311 (95% ДИ 0,918-0,929; p <0,0001).

Выводы. Применение манодебитометрического исследования холедоха с фармакологическим тестом на расслабление Сфинктера Одди позволяет во время операции на 34,8% увеличить выявление причин ВХС при осложненном ХЛ, выявить его дисфункцию и может быть рекомендовано к практическому применению для распознавания типов ВХС, его главных причин и интраоперационного определения показаний для их коррекции во время операции.

Ключевые слова: манодебитометрия, внепеченочный холестаз, осложненный холелитиаз

MANODEBITOMETRY OF EXTRAHEPATIC CHOLESTASIS IN COMPLICATIONS OF CHOLELITHIASIS

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Purpose: to evaluate the effectiveness of the combined method of manodebitometry in intraoperative diagnosis of the causes of various types of extrahepatic cholestasis in complications of cholelithiasis.

Research materials and methods. Manodebitometry was performed in 181 patients who were operated on in the Department of Surgery of the Digestive Organs of the

Institute of Gastroenterology of the Academy of Medical Sciences of Ukraine for the period from 2013 to 2020 using developed software and hardware complex. All patients before surgery were performed: ultrasound, and if choledochocalculosis is suspected − ERCP and MRCP. The motor-evacuatory function of the gallbladder was also assessed.

Results and discussion. Depending on the presence of biochemical markers of jaundice and hepatocyte damage, as well as the presence of predictors of cholestasis in the anamnesis, patients were divided into 5 groups outside of hepatic cholestasis (EHC).

The use of a combined method of manodebitometry in intraoperative diagnosis of the main causes of various types of EHC in complications of cholelithiasis, allowed in 34 (18.78%) patients diagnose organic disorders as the cause of EHC, and in 38 (20.99%) patients − functional disorders of the sphincter Oddi. Carrying out ROC-analysis of application of the combined technique of manodebitometry as diagnostic screening of the functional and organic reason of EHC at complications of cholelithiasis has allowed to establish high quality of diagnostic model with use of determined coefficient as an optimum threshold of classification with accuracy of 88,9%, sensitivity of 93,6%, specificity of 80%, as AUC = 0.9311 (95% CI 0.918-0.929; p <0.0001).

Conclusions. The manodebitometric examination of choledochus during surgery with a pharmacological test for relaxation allows to increase by 34.8% the detection of the causes of EHC in complicated cholelithiasis, identify its dysfunction and can be recommended for practical use for recognizing the type of EHC, its main causes and intraoperative indications for their correction during operation.

Key words:manodebitometry, extrahepatic cholestasis, complicated cholelithiasis

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