

MEDICAL UNIVERSITY – PLEVEN
FACULTY OF HEALTH CARE
DEPARTMENT OF THERAPEUTIC CARE

Doctor GORAN SARAFILOSKI

**INSTRUMENTAL DIAGNOSTIC AND ENDOSCOPIC
THERAPEUTIC PROCEDURES IN EXTRAHEPATIC
CHOLESTASIS**

ABSTRACT

**of a dissertation for the award of an education and scientific degree
„Doctor“
Scientific specialty „Gastroenterology“**

Scientific leader: Assoc.prof. dr. Ivan Anastasov Lalev, MD

Pleven 2020

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Official reviewers:

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Assoc. prof. dr. Vladimir Nikolov Andonov, MD**

Pleven 2020

[2]

This dissertation is written on 173 standart printed pages, it is illustrated with 31 tables and 159 figures. References include 376 titles, of which 36 in Cyrillic and 310 in Latin.

10 publications have been realized in conjunction with the dissertation.

The study was conducted in the Gastroenterology Diagnostic Department at the Gastroenterology Clinic, University Hospital “Dr. Georgi Stranski” – Pleven, where the doctoral student works.

The doctoral student is enrolled in a doctoral program of independent preparation at the department of Nursing Therapeutic Care, Faculty of Health Care, Medical University – Pleven /Order № 1475 from 21.06.2018 of the Rector/.

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The materials on the defense are available on the website of the Medical University – Pleven – www.mu-pleven.bg .

The defense of the dissertation will take place on 16 Dec. 2020, at 13:30 O`clock in Ambroise Pare Hall at the Telecommunication Endoscopy Center (TELETZ) at Medical University of Pleven, at an open meeting of the scientific jury, determined by order № 2358 from . 29.Sep.2020 г.. from the Rector of MU-Pleven.

ABBREVIATIONS USED:

PSC – primary sclerotic cholangitis	ASGE – American Society of Gastrointestinal Endoscopy
AIDS - acquired immune deficiency syndrome	ESGE – European Society of Gastrointestinal Endoscopy
EHC – extrahepatic cholestasis	INR- International normalized ratio
IHC – intrahepatic cholestasis	SEMS – Self-expandable metal stent
US – abdominal ultrasound	SOD- Sphincter of oddi dysfunction
CAT – computerized axilar tomography	
NMRT – nuclear magnetic resonance tomography	
MRC – magnetic resonance cholangiography	
EUS – endoscopic ultrasound	
ERCP-endoscopic retrograde cholangiopancreatography	
PPI – proton pump inhibitors	
PEP – post ERCP pancreatitis	
EST – endoscopic sphincterotomy	
HCC – hepatocellular carcinoma	
CCC – cholangiocellular carcinoma	
NSAIDs – nonsteroidal anti-inflammatory drugs	

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INTRODUCTION

In recent years, the diagnostic and therapeutic approach to diseases of the biliary tract and pancreas, occurring with mechanical obstruction have been the subject of various discussions by gastroenterologists, surgeons, radiologists and oncologists.

Biliary tract disorders affect a significant part of the population, their frequency increases with age approximately the same in both sexes. Extrahepatic cholestasis is a term that means an impaired drainage of the bile ducts caused by a mechanical stop at various levels between the liver and the duodenum or secondarily as a result of external compression.

Clinically, the condition is manifested by yellowing of the skin and visible mucous membranes, darkening of the urine, lightening of the stool, fever and / or pain. The causes can be benign or malignant. The most common causes are choledocholithiasis and malignancies of the bile ducts and pancreas. The etiological causes of extrahepatic cholestasis depending on the site of obstruction are /tabl №1/:

Intrahepatic biliary obstruction	Biliary obstruction at the level of porta hepatis	Biliary obstruction at the level of the common bile duct	Intrapancreatic biliary obstruction, including ampullary
primary sclerosing cholangitis	primary sclerosing cholangitis	pancreatic cancer	pancreatic cancer
metastatic liver	cholangiocarcinoma	metastatic disease	pancreatitis
	gallbladder cancer	pancreatitis	choledocholithiasis
	metastatic disease	iatrogenic obstruction	ampullary stenosis
		cholangiocarcinoma	Ampullary or duodenal cancer
			cholangiocarcinoma

Etiological causes of extrahepatic cholestasis depending on the site of obstruction /tabl №1/:

The treatment of patients with extrahepatic cholestasis is stepwise. The first step is to assess the clinical condition and biochemical parameters. It is followed by the implementation of non-invasive instrumental methods - abdominal ultrasound and, if necessary, computed tomography and magnetic resonance cholangiography.

Endoscopic methods are the gold standard for the diagnosis and treatment of benign and malignant diseases of the hepatobiliary system and pancreas. In advanced malignancies, stent placement ERCP is the preferred palliative method, replacing major surgical interventions with the same success and average patient survival.

PURPOSE AND TASKS

Purpose:

To research the frequency of the causes leading to extrahepatic cholestasis and the possibilities of non-invasive and invasive methods for diagnosis and therapeutic behavior

Tasks :

1. Analysis of the demographic data in patients with diseases leading to extrahepatic cholestasis.
2. Analysis of the frequency and causes leading to extrahepatic cholestasis.
3. To study the diagnostic possibilities of non-invasive instrumental methods in extrahepatic cholestasis.
4. To study the possibilities and effectiveness of ERCP for the diagnosis and treatment of extrahepatic cholestasis according to the level of obstruction.
5. Analyze the causes, frequency and severity of ERCP complications according to the level of obstruction.
6. To propose an optimized diagnostic-therapeutic algorithm of behavior in case of complications of ERCP.

Materials and methods:

Materials:

This is a combined retro- and prospective study, which includes 311 patients of whom 154 men /49.5%/ and 157 women /50.5%/ aged 21-94 years with extrahepatic cholestasis who underwent non-invasive procedures, diagnostic and therapeutic ERCP in GDD for a period of 4 years /01.05.2014 – 30.04.2018/.

All of the patients were hospitalized in Hepatogastroenterology department and Surgery departments in UMHAC. The group of studied patients is heterogenous, unselected and represents the real pathology in all its aspects. They were referred for diagnostic clarification and endoscopic treatment. The distribution of patients by clinical departments is presented in table 2.

	number of patients	%
Hepatogastroenterology Department	55	17,7
Surgery Departments	256	82,3

Table № 2 Distribution of patients by clinical departments (n = 311)

According to the requirements of the ethics committee in MU- Pleven, all of the patients have been informed in writing about the algorithm of performing the diagnostic investigations, treatment and possible complications that may occur. The personal data of the patients and results from the investigations were stored, processed and presented in accordance with the Personal Data Protection Law.

Methods:

1. Diagnostic methods:

1.1. Clinical methods:

1.1.1. Medical history

1.1.2. Physical status

1.2. Laboratory methods:

1.3. Instrumental methods:

1.3.1. Abdominal ultrasound

1.3.2. Computed axial tomography

1.3.3. Magnetic resonance cholangiography

1.3.4. Endoscopic retrograde cholangiopancreatography

2. Therapeutic methods:

2.1. Conservative treatment.

Pre-endoscopic treatment – it was performed with insertion of naso-gastric tube, zero diet, intravenous antispasmodics, PPIs, antibiotics, hepatoprotectors, blood transfusions, NSAID suppositories. In case of impaired hemostasis, infusion of fresh frozen plasma, vitamin K and platelet mass was performed. Patients on anticoagulant therapy were switched to low molecular weight heparin.

2.2. Endoscopic retrograde cholangiopancreatography / ERCP /

It was performed in 307 patients studied. Indications for its implementation were clinical, biochemical and data from non-invasive instrumental investigations for extrahepatic cholestasis. ERCP has two important aims:

1. Diagnose - dilated common bile duct and intrahepatic bile ducts are visualized after contrast.
2. Endoscopic treatment conducting.

This diagnostic/therapeutic procedure was performed up to 72 hours after hospitalization on an empty stomach under general anesthesia supervised by a team of anesthesiologist and nurse.

Surgery

Patients were referred for surgical treatment after unsuccessful ERCP in order to provide bile drainage or in a case of post-ERCP complication.

3. Statistical methods:

The data was entered and processed with the statistical package SPSS 24.0 and Excel for Windows. For a significant level at which the null hypothesis was rejected, $p < 0.05$ was chosen.

RESULTS:

1. Demographic data of patients with diseases leading to extrahepatic cholestasis. The data of 311 patients with extrahepatic cholestasis was analyzed in DGD for a period of 4 years. 154 were men (49.5%) and 157 women (50.5%) (Figure №1).

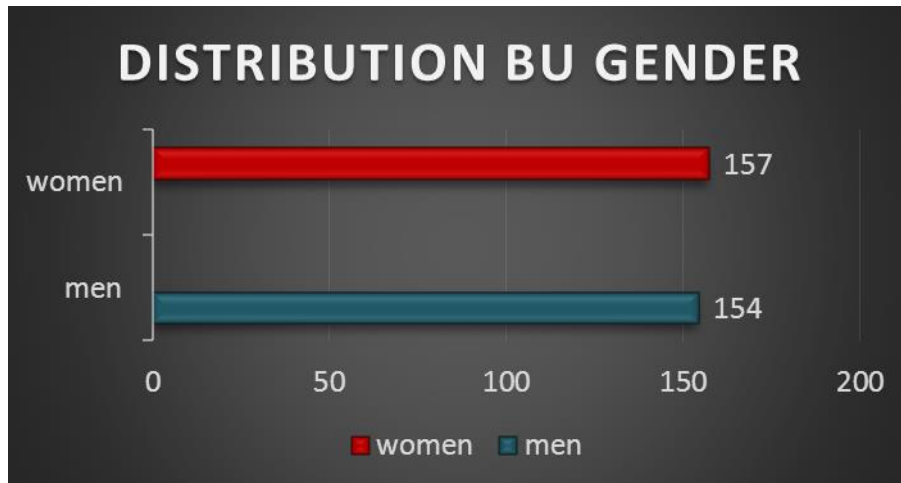


Figure. № 1 Distribution of patients by gender (n = 311)

According to age criterion, the patients were divided into 9 groups /age intervals in 10 years/. (Figure №2).

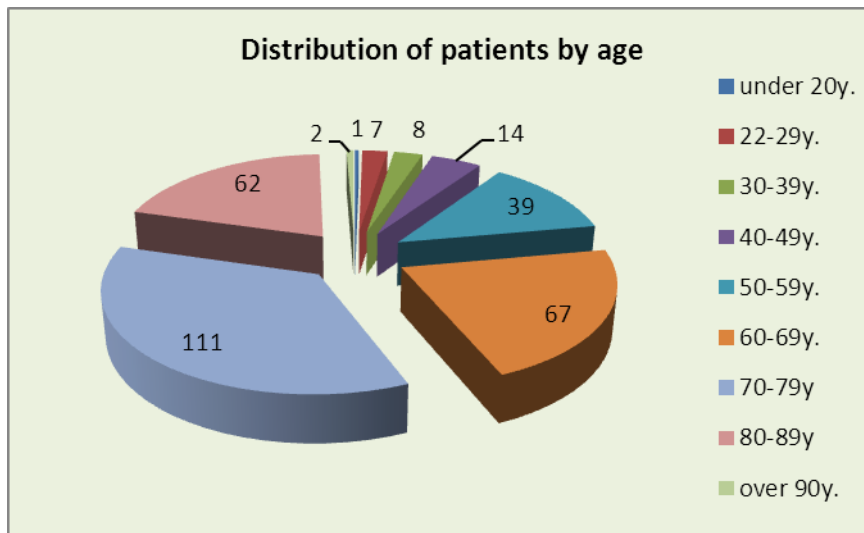


Figure. №2 Distribution of patients by age (n = 311)

The average age of the patients was 68.24 years (standard deviation 14.129), ranging from 19-92 years. The histogram of age distribution at admission showed that the majority of patients were between 60 and 89 years of age

(77.2%). Females predominated in the younger age groups, and males - in the older age groups. There were no significant differences in the percentage of men and women in the age ranges.

2. Analysis of the frequency and causes leading to extrahepatic cholestasis

In all patients, the final diagnosis was made on the basis of clinical symptoms, laboratory tests, instrumental diagnostic methods /abdominal ultrasound in 311 patients, CAT in 203 patients, MRC in 29 patients, ERCP in 307 patients/, pathoanatomical examination and surgical treatment in 30 patients. The presence of jaundice and/or abdominal pain was the main indication to provide laboratory and non-invasive imaging instrumental clinical investigations. From the laboratory tests the rates of amylase, cholestasis enzymes (alkaline phosphatase, gamma-glutamyl transferase) and total and direct bilirubin had the biggest value. They were significantly elevated from the normal rates and were statistically significant ($p < 0.05$).

In the processing and analysis of the results from diagnostic methods, patients were grouped and studied in two particular areas:

- According to the level of obstruction of the pathological process in the bile ducts according to the classification of Kurochka et al;
- According to the type and nature of the pathological process – benign and malignant

Analysis of the results in 311 patients with extrahepatic cholestasis according to the level of biliary tract obstruction.

The distribution of patients with mechanical jaundice, according to the level of obstruction and etiological causes in the biliary tract according to the classification of Kurochka et al. is presented in table № 3.

Intrahepatic biliary obstruction	Biliary obstruction at the level of porta hepatis	Biliary obstruction at the level of the common bile duct	Intrapancreatic biliary obstruction, including ampullary
	Klatskin tumor - 11 patients /3,5%/	Pancreatic cancer- 54 patients /17,4%/	Ampullary stenosis- 40 patients/12,9%/
	Gallbladder cancer - 5 patients /1,6%/	Choledocholithiasis- 120 patients /38,6%/	Choledocholithiasis - 12 patients /3,8%/
	Echinococcal cyst compression -1 patient /0,3%/	Cholangiocarcinoma- 17 patients /5,5%/	Ampullary cancer- 8 patients /2,6%/
		Iatrogenic obstruction- 6 patients/1,9%/	Peripapillary duodenal diverticulum – 2 patients /0,6%/
		Metastatic cancer - 3 patients / 1% /	Pancreatic pseudocyst -1 patient/0,3%/
		Benign stenosis – 5 patients / 1,6% /	Acute pancreatitis - 26 patients /8,4%/
		205 patients 65,9%	89 patients 28,6%
	17 patients 5,5%		

Table № 3 Distribution of patients with mechanical jaundice according to the level of obstruction in the biliary tract (n=311)

17 /5.5%/ of 311 patients had an obstruction at the level of porta hepatis. In the group studied females prevailed – 12 patients/70.9%/, to males – 5 patients /29.1%/. 12 patients /70.9%/ were over the age of 60 years old. The most common causes are presented in Table № 4.

Diagnosis	patients	%
Klatskin tumor	11	64,7%,
Gallbladder cancer	5	29,4%
Echinococcal cyst compression	1	5,9%
Total	17	100%

Table №4 Distribution at the level of porta hepatis (n=17)

205 /65.9%/ of 311 patients had an obstruction at the level of the common bile duct. In the group studied males prevailed – 107 patients /52.2%/ to females – 98 patients /47.8%/. 172 patients /83.9%/ were over the age of 60 years old. The most common causes are presented in Table № 5.

Diagnosis	patients	%
Choledocholithiasis	120	58,5%
Pancreatic cancer	54	26,3%
Cholangiocarcinoma	17	8,3%
Iatrogenic obstruction	6	2,9%
Benign stenosis	5	2,4%
Metastatic cancer	3	1,5%
Total	205	100%

Table № 5 Distribution at the level of the common bile duct (n=205)

89 /28.6%/ of 311 patients had an intrapancreatic/ampullary biliary obstruction. In the group studied females prevailed – 46 patients /51.7%/, to males – 43 patients /48.3%/. 60 patients /67.4%/ were over the age of 60 years old. The most common causes are presented in Table № 6.

Diagnosis	Patients	%
Ampullary stenosis	40	44,9%
Acute pancreatitis	26	29,2%
Choledocholithiasis	12	13,5%
Ampullary cancer	8	9%
Peripapillary duodenal diverticulum	2	2,2%
Pancreatic pseudocyst	1	1,1%
Total	89	100%

Table №6 Distribution at intrapancreatic/ampullary level (n=89)

According to the type of pathological process, patients were divided into two groups – benign and malignant:

Benign causes were diagnosed in 213 patients /68.5%/ (figure №3), of which:

- ✚ Cholelithiasis - 132 patients /42,4%/;
- ✚ Sclerosing papilloiditis - 40 patients /12,9%/;
- ✚ Compression of the common bile duct - 4 patients /1,3%/:
 - Cysts – 2 patients /0,64%/;
 - Peripapillary duodenal diverticulum – 2 patients /0,64%/;
- ✚ Benign stenosis - 5 patients /1,6%/;
- ✚ Iatrogenic after surgical complication - 6 patients /1,9%/;
- ✚ Pancreatitis - 26 patients /8,4%/ ;

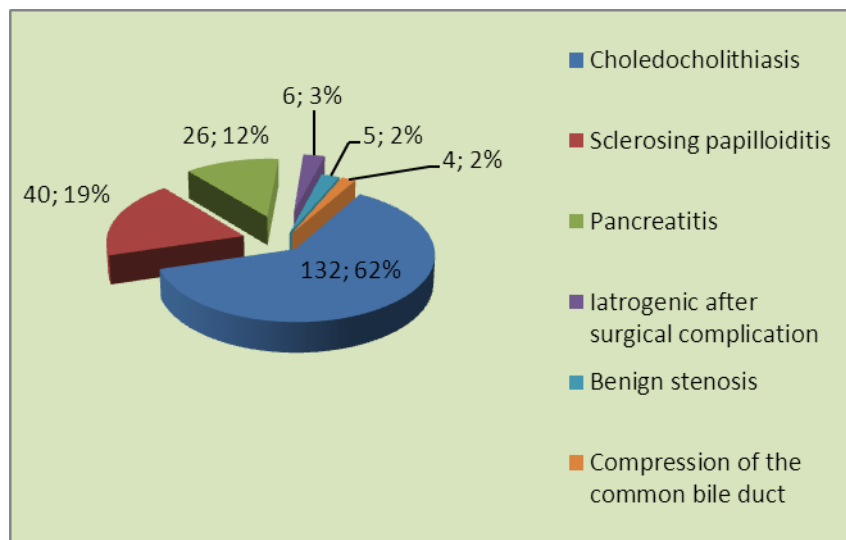


Fig.№3 Extrahepatic benign causes (n=213)

There were 98 patients /31.5%/ with malignant genesis (figure №4), of which:

- ✚ Perihepatic bile duct stenosis - 16 patients /5,1%/ of which:
 - Gallbladder cancer - 5 patients /1,6%/;
 - Klatskin tumor - 11 patients /3,5%/;
- ✚ Distal stenosis of the common bile duct - 74 patients /23,8%/:
 - Cholangiocarcinoma - 17 patients /5,5%/;
 - Pancreatic cancer - 54 patients /17,4%/;
- ✚ Ampullary cancer - 8 patients /2,6%/ ;
- ✚ Compression of the common bile duct by enlarged lymph nodes - 3 patients /0,96%/.

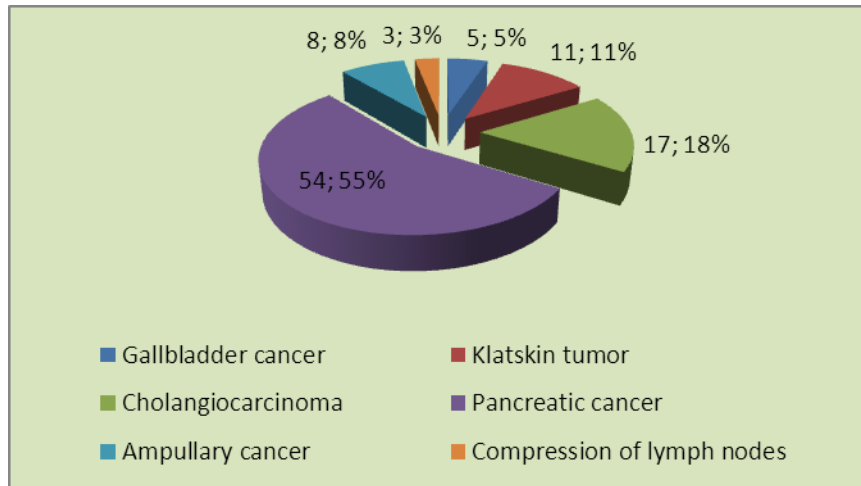


Fig. №4 Extrahepatic malignant causes (n=98)

Distribution of all the patients with extrahepatic cholestasis by diagnosis

The most common causes of extrahepatic cholestasis in the 311 patients studied was choledocholithiasis – 132 /42.4%/, followed by malignancies – 98 / 31.5%/. These results coincide with the data from the literature. (Fig. №5)

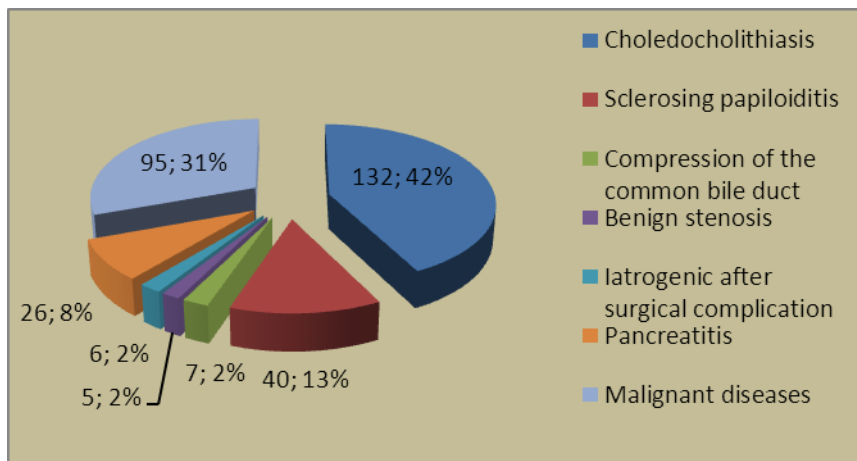


Fig №5 The most common causes of extrahepatic cholestasis (n=311)

3. Diagnostic possibilities of the non-invasive instrumental methods in extrahepatic cholestasis

3.1. Ultrasound diagnosis in patients with extrahepatic cholestasis

Ultrasound was used as the first instrumental method in all 311 patients with extrahepatic cholestasis. It was performed within 24 hours of hospitalization. The main criteria for diagnosis were dilatation of the intrahepatic bile ducts, dilated common bile duct, gallbladder hydrops with or without stones, tumor formation of the bile ducts and in the area of the head of the pancreas. The diagnostic potential of ultrasound depending on the level of biliary tract obstruction according to Kurochka's classification were studied and analyzed. Patients were divided into three groups:

- ✚ Obstruction at the level of porta hepatis;
- ✚ Obstruction at the level of the common bile duct ;
- ✚ Obstruction at intrapancreatic/ampullary level

17/5.5%/ of all the 311 patients had an obstruction at the level of porta hepatis. A coincidence of the ultrasound diagnosis with the final one was found in 9 patients /52.9%/. The diagnostic capabilities of ultrasound are presented in Fig. № 6.

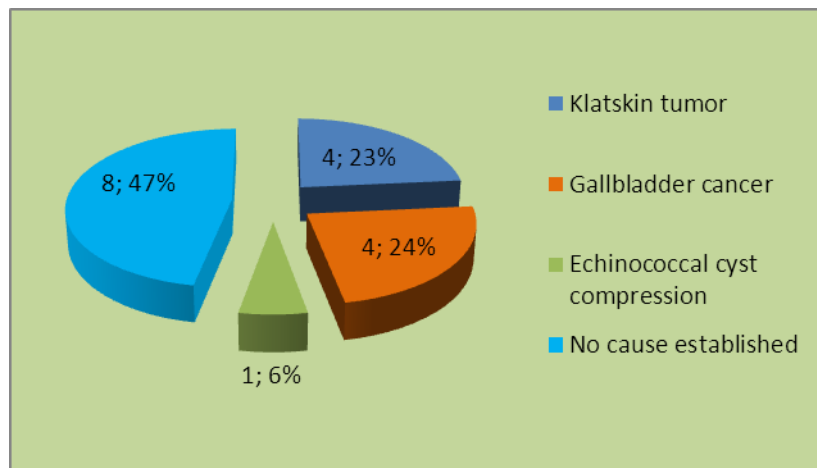


Fig.№ 6 Ultrasound findings at the level of porta hepatis (n=17)

In 8 patients /47.1%/ the diagnosis was compromised:

- one patient /5,9%/ with gallbladder cancer was diagnosed with chronic calculous cholecystitis.
- Four /23,5%/ patients with a final diagnosis of Klatskin tumor were found to have only dilated intrahepatic bile ducts and normal gallbladder and common bile duct, and one patient with Klatskin tumor was diagnosed with a gallstone in the common hepatic duct.

- two /11, %/ patients were not found to have dilated intrahepatic bile ducts during the examination.

The sensitivity of the ultrasound examination in our case for extrahepatic cholestasis at the level of porta hepatis was 88.2%, the specificity - 52.9%.

205 /65.9%/ of all the 311 patients had an obstruction at the level of the common bile duct. A coincidence of the ultrasound diagnosis with the final one was found in 172 patients /83,9%/. The diagnostic capabilities of ultrasound are presented in Fig. № 7.

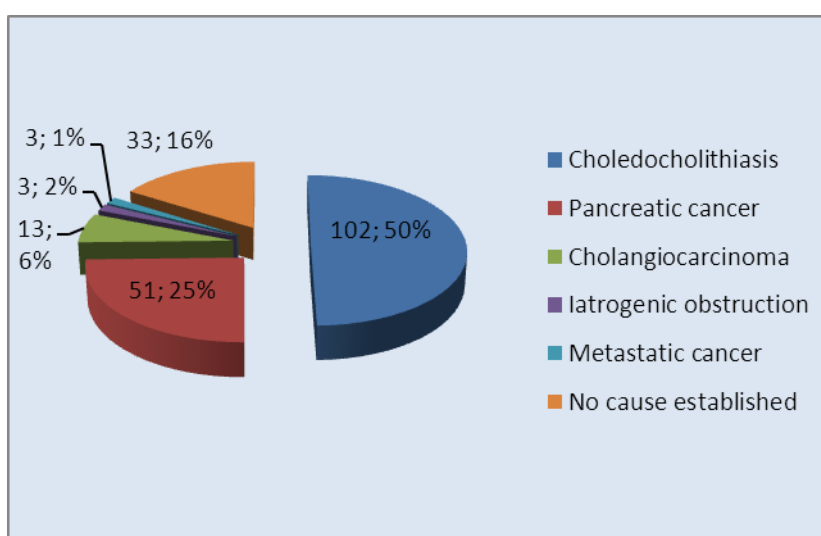


Fig.№ 7 Ultrasound findings at the level of the common bile duct (n=205)

In 33 patients /16,1%/ the diagnosis was compromised:

Three patients with pancreatic cancer were not diagnosed by ultrasound due to gas collections, which made the visualization of the organ difficult. In 21 patients the distal third of the common bile duct was not imaging. They had a definitive diagnosis:

- benign stenosis – 5 patients
- cholelithiasis – 12 patients
- cholangiocarcinoma – 4 patients

In 9 patients of which 6 with cholelithiasis and 3 with iatrogenic injury, dilated intrahepatic bile ducts were not found at the time of the examination.

The sensitivity of the ultrasound examination for extrahepatic cholestasis at the level of the common bile duct in our case was 96%, the specificity – 83.9%.

89 /28,6%/ of all the 311 patients had an extrahepatic cholestasis at an intrapancreatic/ampullary level. A coincidence of the ultrasound diagnosis with the final one was found in 21 patients /23,6%/. The diagnostic capabilities of ultrasound are presented in Fig. № 8.

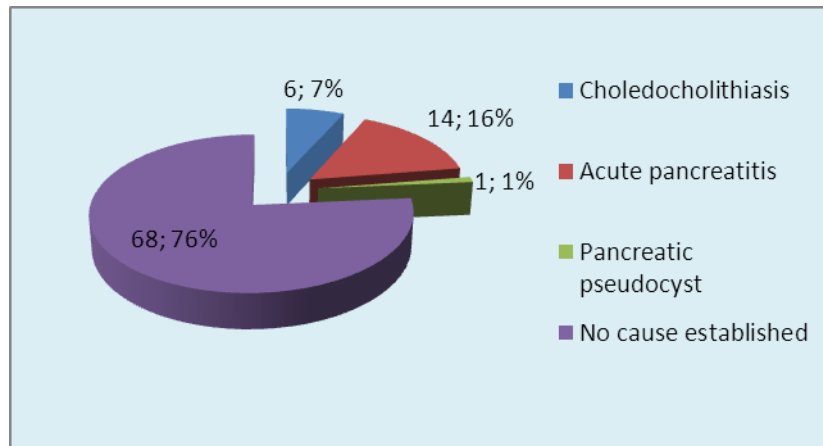


Fig.№8 Ultrasound findings in intrapancreatic/ampullary area (n=89)

In 68 patients /76,4%/ the diagnosis was not established.

In 6 /6,7%/ of them the stones were located peripapillary.

In 23 /25,8%/ patients due to the presence of gas collections and difficult examination in this area the cause of obstruction was not found. They had a definitive diagnosis:

- Ampullary cancer – 8 patients;
- peripapillary duodenal diverticulum – 2 patients;
- sclerosing papiloiditis – 13 patients.

In 39 patients /43,8%/ - 12 with pancreatitis and 27 with sclerosing papiloiditis, dilated intrahepatic bile ducts were not visualized at the time of abdominal ultrasound.

The sensitivity of the ultrasound examination for extrahepatic cholestasis at the intrapancreatic/ampullary level was 56,2%, the specificity – 23.6%.

A definitive ultrasound diagnosis of extrahepatic cholestasis with various etiologies and dilated intrahepatic bile ducts and common bile duct, was found in 261 of 311 patients. The diagnostic value (sensitivity) of the abdominal ultrasound was 84%. Dilated intrahepatic bile ducts were not detected in 50 patients /16%/ on first ultrasound, despite of the clinical and biochemical data for extrahepatic cholestasis. The exact etiological cause was found in 202 patients. The specificity of the ultrasound examination was 65%. The most common ultrasound-identified cause was choledocholithiasis in 108 patients /34,7%/, followed by malignancies in 75 patients /24,1%/. (fig.№ 9-11)

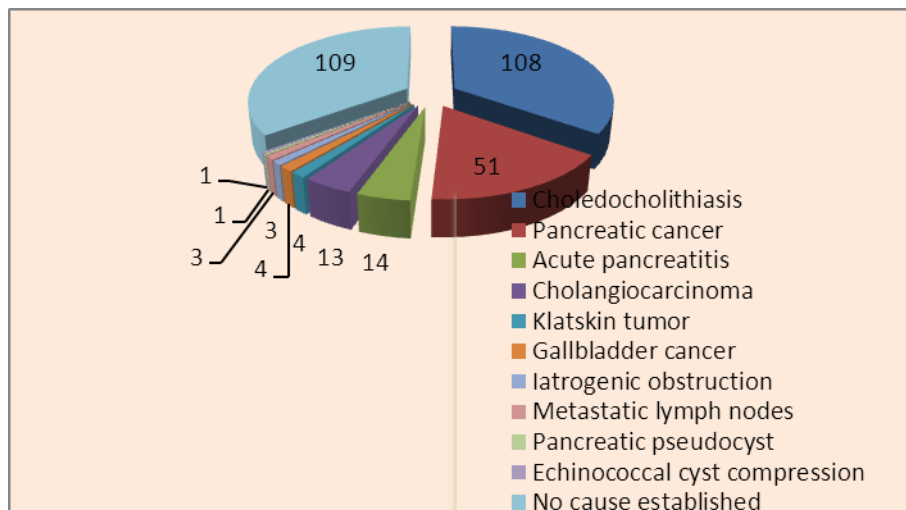


Fig.№9 Causes of extrahepatic cholestasis proved by ultrasound (n = 311)



Fig.№10



Fig.№11

Ultrasound-identified gallstones in the common bile duct

3.2. Diagnostic potential of Computerized Axial Tomography

CAT was performed in 203 /65.3%/ of 311 patients in cases of unclear cause of obstructive jaundice, in patients with suspected evidence of malignant stenosis of the biliary tract or to confirm the ultrasound finding. 108 patients in whom ultrasound revealed choledocholithiasis were excluded from this group.

The results of CAT were analyzed depending on the location and level of obstruction in the extrahepatic biliary system according to Kurochka's classification. 17 /5,5%/ of 311 patients had an obstruction at the level of porta hepatis. An accurate diagnosis in this group was made in 14 patients /82,4%/. The distribution of patients by diagnoses is presented in Fig. № 12

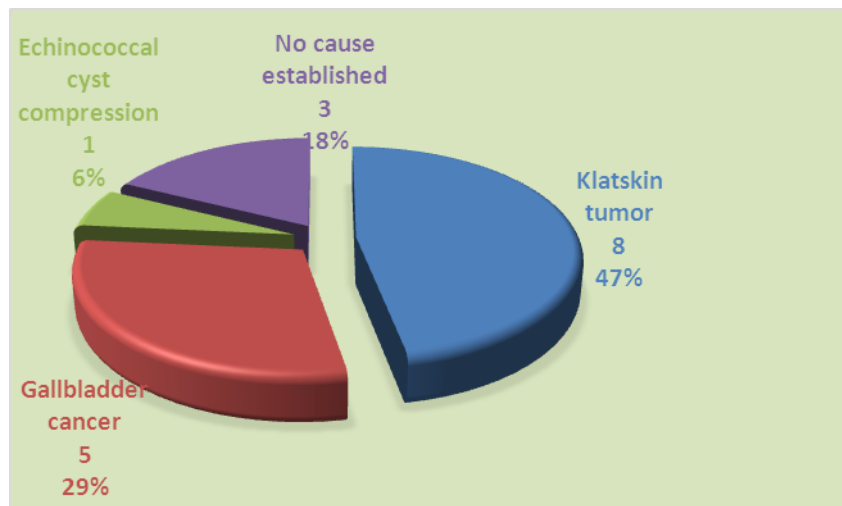


Fig.№12 CAT findings at the level of porta hepatis (n=17)

In 3 /17,6%/ patients Klatskin tumor was suspected due to dilated intrahepatic bile ducts and normal common bile duct, but tumor formation was not visualized on CAT.

The sensivity of computed tomography established by us for detection of extrahepatic cholestasis at the level of porta hepatis is 100%, the specificity – 82,4%.

205/65,9%/ of 311 patients had an obstruction at the level of the common bile duct. CAT was performed in 103 patients. A coincidence of CAT diagnosis with the final one was found in 89 patients /86,4%/. The diagnostic capabilities of CAT was presented in fig. №13 .

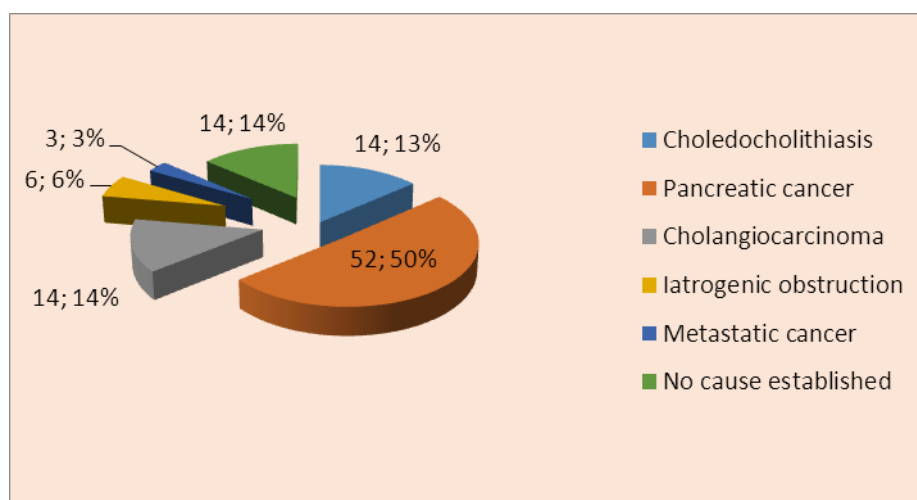


Fig.№13 CAT findings at the level of the common bile duct (n=103)

According to the localization of the cause of biliary obstruction at the level of the common bile duct using CAT we found:

- Iatrogenic injury of the common bile duct after cholecystectomy in 6 patients /100%/.
- The presence of metastatic lymph nodes compressing and/or infiltrating the common bile duct in 3 patients /100%/;
- Pancreatic cancer in 52 patients /96,3%/;
- Cholangiocarcinoma in 14 patients /76,3%/;
- Choledocholithiasis in 14 patients /77,8%/ from 18 CAT performed.

The exact cause of extrahepatic cholestasis was not established in 14 patients /13,6%/.

Four of them had small stones located in the distal third of the common bile duct.

In 8 patients – 3 with cholangiocarcinoma and 5 with benign stenosis there was an evidence of dilated intrahepatic bile ducts and common bile duct, without an exact cause established.

In 2 patients no evidence of obstruction was found at the time of CAT.

The sensitivity of computed tomography established by us for detection of extrahepatic cholestasis at the level of the common bile duct is 98%, the specificity – 86,4%.

89 /28,6%/ of 311 patients had an obstruction at the intrapancreatic/ampullary level. CAT was performed in 83 patients. A coincidence of CAT diagnosis with the final one was found in 30 patients /36,1%/. The diagnostic capabilities are presented in fig. №14

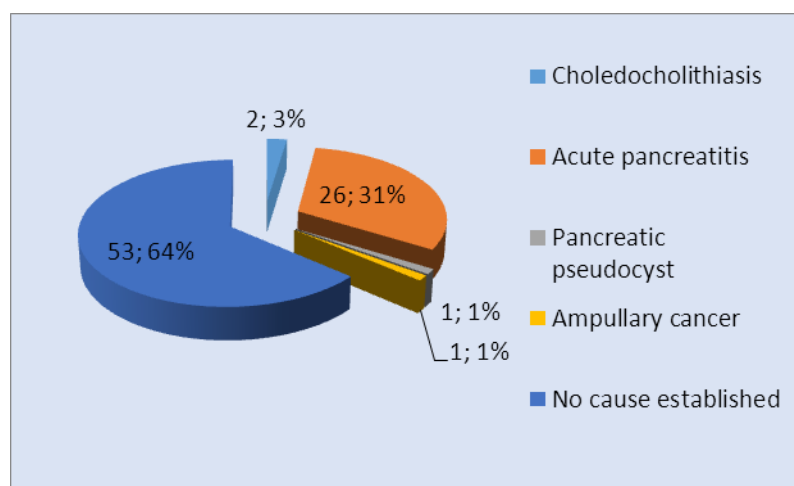


Fig.№14 CAT findings at intrapancreatic/ampullary level (n=83)

According to the localization of the cause of biliary obstruction in the intrapancreatic/ampullary level, using CAT we found:

- Pancreatic pseudocyst in one patient /100%/;
- Acute pancreatitis in 26 patients /100%/;
- Peripapillary located stones in 2 patients /33,3%/, from 6 CAT performed;
- Papilla of Vater cancer in one patient /12,5%/.

In 53 /63,8 %/ patients the diagnosis was compromised.

- 29 /54,7%/ of them were with dilated intrahepatic bile ducts and common bile duct without defects in their lumen
- In 8 /15,1%/ patients choledocholithiasis was found
- In 16 /30,2%/ patients no data for obstruction was found at the time of CAT performing.

The sensitivity of computed tomography established by us for detection of extrahepatic cholestasis at intrapancreatic/ampullary level is 80,7%, the specificity – 36,1%.

A definitive CAT diagnosis of extrahepatic cholestasis with various etiologies and dilated intrahepatic bile ducts and common bile duct was found in 185 of 203 patients. The diagnostic value /sensitivity/ for detecting obstructive jaundice was 91,1%. In 18 /8,9%/ patients dilated intrahepatic bile ducts were not detected, despite of clinical and biochemical evidences of extrahepatic cholestasis. The exact etiological cause was found in 133 patients. The specificity is 65,5%. The most common CAT-identified causes were malignant diseases in 83 /62,4%/ patients. (fig. №15)

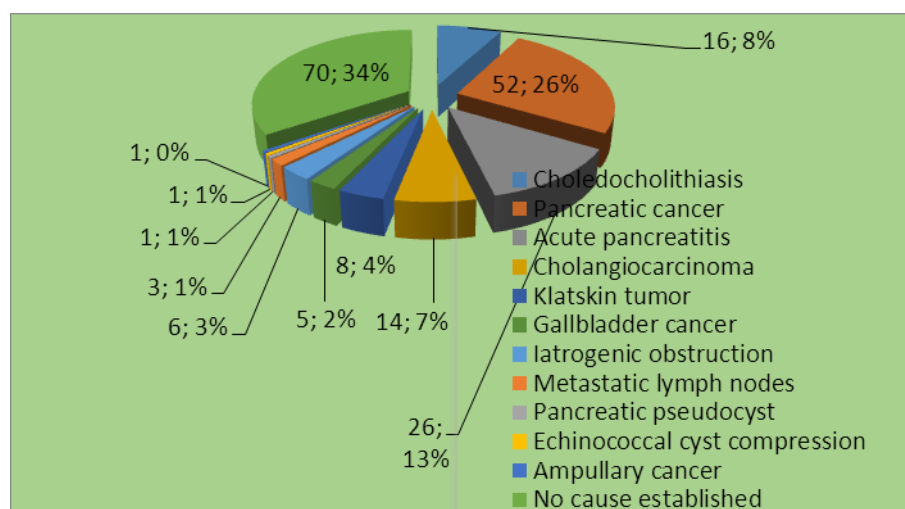


Fig.№15 CAT identified causes for extrahepatic cholestasis (n = 203)

3.3. Diagnostic potential of Magnetic Resonance Cholangiography

Magnetic resonance cholangiography (MRC) was used as a step in imaging diagnostic in patients with extrahepatic cholestasis after ultrasound and computed tomography were performed. The study was performed in 29 /9,3%/ of all 311 patients. In 25 patients MRC was performed before ERCP to determine the condition of the biliary tract in view of forthcoming endoscopic and surgical interventions. Distribution of patients according to the diagnosis and the level of the obstruction of the process is presented in tab. № 7

Level of obstruction	Total number of patients	MRC	Exact diagnosis
Porta hepatis	17	11	Klatskin tumor - 11
Common bile duct	205	14	Cholelithiasis -4 Cholangiocarcinoma - 5 Benign stenosis - 5

Table № 7

In 4 of them we performed MRC as a subsequent stage of the diagnostic process after unsuccessful ERCP and to confirm the finding.

- 2 patients with pancreatic tumor
- 2 patients with iatrogenic injury of the common bile duct after cholecystectomy

4. Possibilities and effectiveness of ERCP for diagnosis and treatment of extrahepatic cholestasis.

Indications for performing ERCP in our patients were the cholestasis constellation and the data for extrahepatic cholestasis from imaging studies.

ERCP was performed of 307 of all the 311 patients. Four of the patients refused the procedure and were referred to other endoscopic centers.

From 307 ERCPs performed, successful cannulation of the common bile duct was achieved in 279 patients /90,9%/, and in 28 /9,1 %/ it was unsuccessful /tab. № 8/.

ERCP	patients	%
successful	279	90,9
unsuccessful	28	9,1
total	307	100

Table № 8

The diagnostic and therapeutic capabilities of ERCP were analyzed depending on the location and the level of obstruction in the extrahepatic biliary system according to Kurochka classification.

ERCP was performed in 16 of 17 patients with an obstruction at the level of porta hepatis. One of the patients with Klatskin tumor refused ERCP. A coincidence of ERCP diagnosis with the final one was found in 14 patients. Diagnostic possibilities are presented in fig. №16

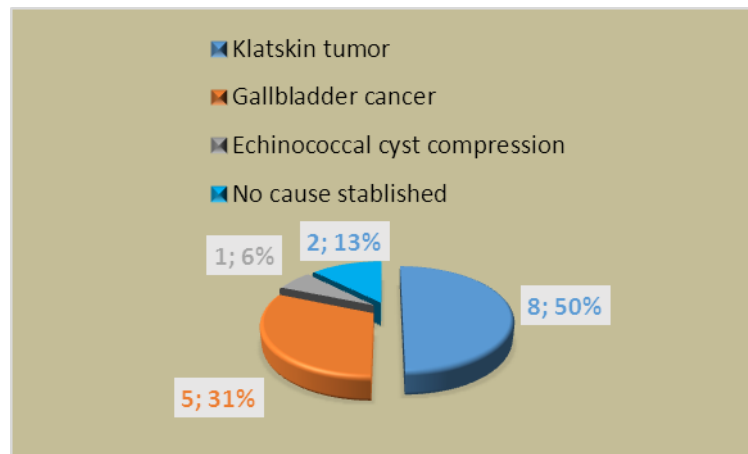


Fig.№ 16 ERCP finding at the level of porta hepatis (n=16)

- In 8 /50%/ of the patients with Klatskin tumor, when contrasting the biliary tract we found incomplete stenosis with unclear outlines at the level of the common hepatic duct without affecting the bifurcation of the right and left hepatic ducts – type I in Bismuth classification. A brush biopsy was performed on the stenotic site. In 2 patients the cytological result proved the presence of tumor cells. In the rest of the patients we received false negative results. The combination of the findings from the non-invasive and invasive procedures gave grounds for the Klatskin tumor diagnosis. We performed prosthetics in 6 patients using a plastic stent 10-12sm 10f., and we inserted a self-expanding metal stents, 10sm in lenght, 10mm lumen in two patients (fig.№ 17-18).

In 2 /12,5%/ of the patients the diagnosis was not initially established. A rounded shadow fixed to the wall was seen after contrasting the common hepatic duct and the intrahepatic ducts, it was reported as a concrement. We performed a papillospincterotomy and a ballon-extractor was inserted, but concrements was not evacuated. Based on a brush biopsy that proved the presence of tumor cells, Klatskin tumor was diagnosed. We inserted plastic stents in these two patients.

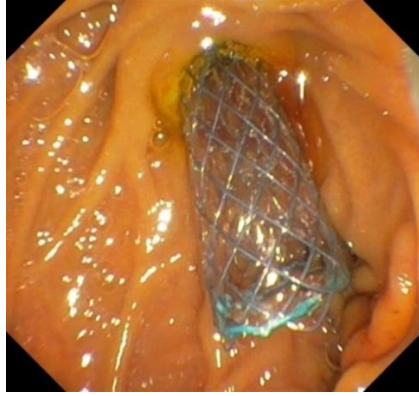


Fig.№ 17

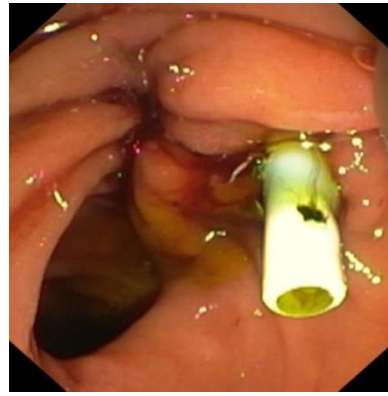


Fig.№ 18

- In 5 /31,3%/ patients who was diagnosed with gallbladder cancer, we found a stenosis in the proximal third of the common bile duct, at the site of infusion of the cystic duct into the common hepatic duct. Four of them had dilated intrahepatic bile ducts, and in one they were normal. One of them had a previous cholecystectomy with histological result of gallbladder cancer, and four had an ultrasound and CAT data for gallbladder cancer. We performed prosthetics if the common bile duct with a plastic stent 10sm 10f in these 5 patients.

- In 1 /6,2%/ patient who was diagnosed with having echinococcal cyst of the liver, a stenosis with smooth outlines was seen when contrasting the common hepatic duct and part of the right hepatic duct. Based on ultrasound and CAT data and the ERCP findings, it was reasonable to think of compression by an echinococcal cyst. We performed prosthetics with a plastic stent. The sensitiviry of ERCP at the level of porta hepatis for the detection of extrahepatic cholestasis was 93,7%, the specificity – 87,5%.

In case of an obstruction at the level of the common bile duct, diagnostic/therapeutic ERCP was performed in 203 /99%/ of the patients. Two of the patients refused ERCP and were referred to other endoscopic centers. At the level of the common bile duct ERCP was successful in 175 /86,2%/ patients. A coincidence of ERCP with the final diagnosis was found in 169 of them /96,6%/. The diagnostic possibilities are presented in fig. № 19

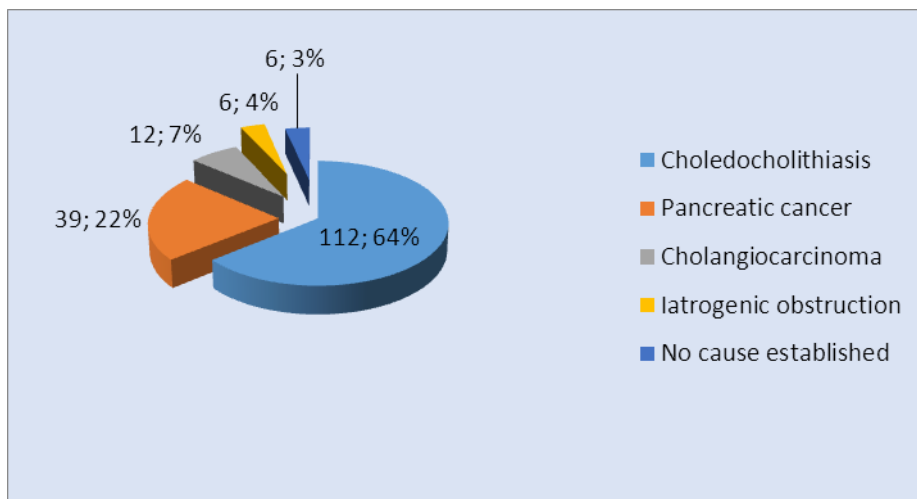


Fig.№ 19 ERCP findings at the level of the common bile duct (n=175)

In the cases of biliary obstruction at the level of the common bile duct we found:
 - In 112 /64%/ patients diagnosed with choledocholithiasis, we found single or multiple concrements in different sizes 4-30mm, when contrasting the bile ducts. (fig.№ 20-21) In three /1,7%/ of them the common bile duct and the intrahepatic bile ducts were normal in size.



Fig. № 20

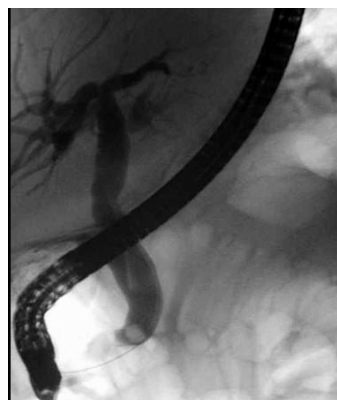


Fig. № 21

X-ray image of a concrement in the common bile duct

We performed a papillosphincterotomy. In 7 /4%/ of the patients the concrements spontaneously migrated into the duodenum after the incision was made and in the rest we used a balloon-extractor (fig №22-23) or a Dormia basket (fig.№ 24-25) .

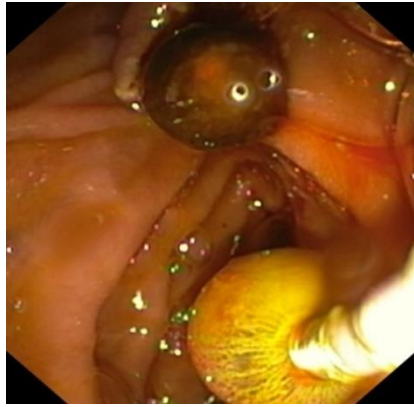


Fig. № 22

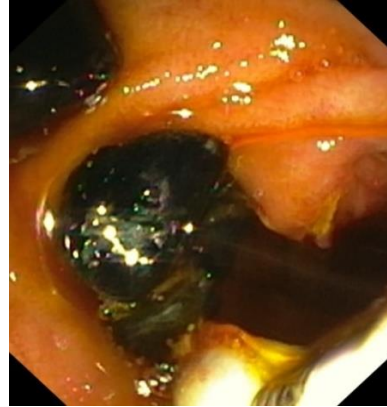
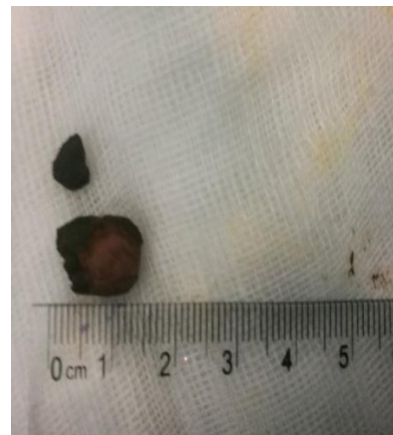


Fig. № 23

Extraction of concrements with balloon-extractor.



Fig.№ 24



Фиг.№ 25

Extraction of concrements with Dormia basket

In 8 /4,5%/ patients the concrement was about 17-20mm in size. We used a Dormia basket and a mechanical lithotripter to break it up. The parts of the stones were evacuated using a balloon-extractor (фиг.№ 26)

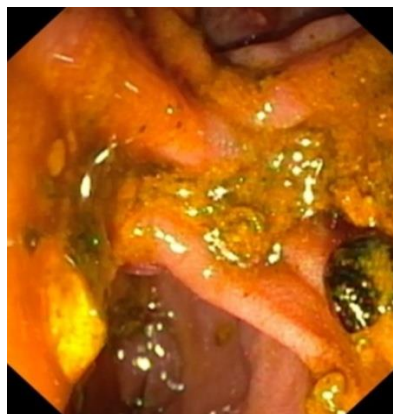


Fig.№ 26 Evacuation of concrements after lithotripsy

In 2 patients a concrement with a diameter over 30mm was seen in the common bile duct. Due to the impossibility of mechanical lithotripsy, a plastic stent was

placed to provide drainage of bile. The patient was referred to choledochoscopy and lithotripsy in other endoscopic centers (fig.№ 27-28)

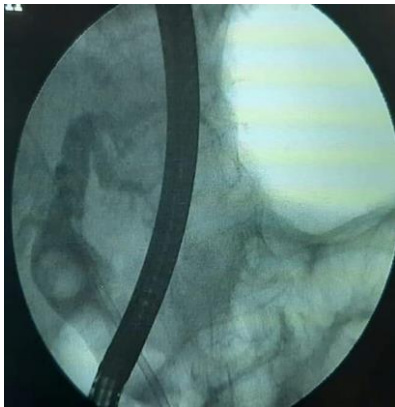


Fig.№27

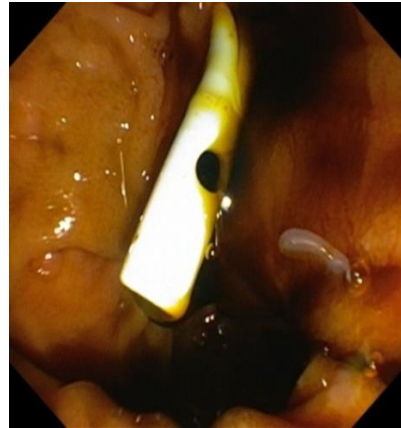


Fig.№28

A plastic stent inserted in choledocholithiasis

In 4 /2,3%/ patients due to a persistence of an obstructive jaundice, a repeated ERCP was performed which found residual concretions. We definitively extracted them.

In 6 patients /3,4%/ due to the small size of the concretions located in the distal third of the common bile duct, they were not detected after contrasting the bile ducts. Concretions were evacuated after a papilloshpincterotomy and insertion of a balloon-extractor.

Different types of concretions were extracted from the common bile duct /endoscopic image/. (fig. № 29 -32)



Fig. № 29

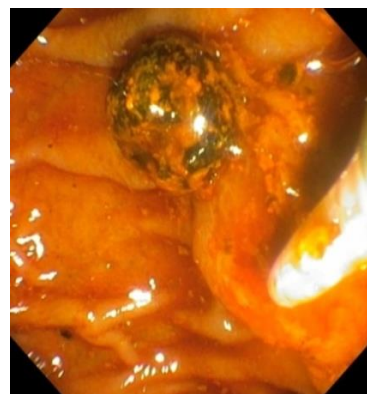


Fig.№ 30



Fig. № 31



Fig. № 32

- 39 /22.3%/ of the patients were definitely diagnosed with pancreatic cancer. We saw an incomplete stenosis when contrasting the distal third of the common bile duct. In eleven patients biopsies from the papilla of Vater were taken and they showed infiltration from the tumor. In 9 patients brush biopsy was made and the cytological result proved the presence of tumor cells, and in the rest we received a false negative result. The combination with the findings of imaging techniques and ERCP, gave rise to the diagnosis of pancreatic cancer. A plastic 6 cm 10f stent was placed in 34 patients, and a self-expanding metal stent (SEMS) - 6 cm long, lumen - 10mm - in 5 patients. The bile contents were successfully drained after stent placement. (fig.№ 33-36)



Fig.№ 33

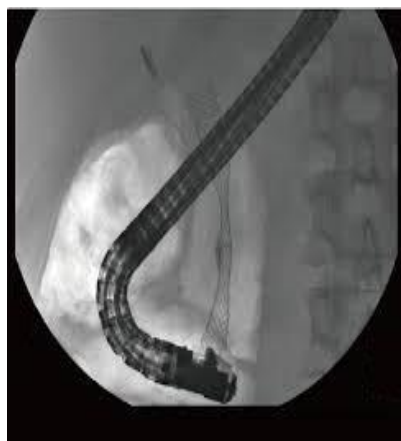


Fig.№34

Stents placed



Фуз.№ 35
X-ray image of a plastic stent



Фуз.№ 36
X-ray image of SEMS

12 /6,9%/ patients were diagnosed with cholangiocarcinoma. An incomplete stenosis was found in the distal and the middle third of the common bile duct after contrasting the bile ducts. The contrast material was passing a thin stream and was coloring the intrahepatic bile ducts. A brush biopsy was performed on the stenotic section. In 5 of 12 patients, a cytological result proved the presence of tumor cells. ERCP findings and the absence of other established formations by imaging methods gave rise to the diagnosis cholangiocarcinoma. We performed successful stenting of the common bile duct with plastic stents 6sm, 10f. (fig.№ 37-38).



Fig.№ 37

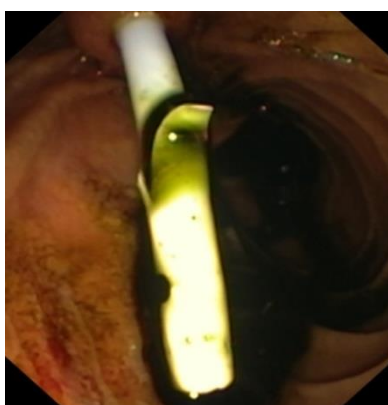


Fig.№ 38

Plastic stents

6 /3.4%/ of the patients were definitively diagnosed with iatrogenic injury of the common bile duct after cholecystectomy

When contrasting the bile ducts in 2 of the patients we found an incomplete stenosis of the common bile duct. The imposed metal clip on the common bile duct was also visualized. Plastic stents were placed in the right and left hepatic duct. In another 2 patients, contrast of the bile ducts revealed that the contrast material entered the bed of the removed gallbladder and stained the transhepatic drain. We placed a plastic stent that passed over the cystic duct. In two patients,

a complete stenosis of the common bile duct from the imposed clip during cholecystectomy was established, after staining the bile ducts.

The established sensitivity of ERCP at the level of common bile duct for detection of extrahepatic cholestasis is 98.3%, the specificity - 96.6%.

In unsuccessful 28 /9.1%/ ERCP, the diagnosis was confirmed by non-invasive instrumental methods - abdominal ultrasound, computed tomography, MRI-cholangiography and surgical treatment with histological verification of malignant diseases.

Out of all 203 patients with extrahepatic cholestasis at the level of the common bile duct, 30 /14.7%/ patients underwent surgical treatment. The distribution by diagnoses is presented in fig. №39

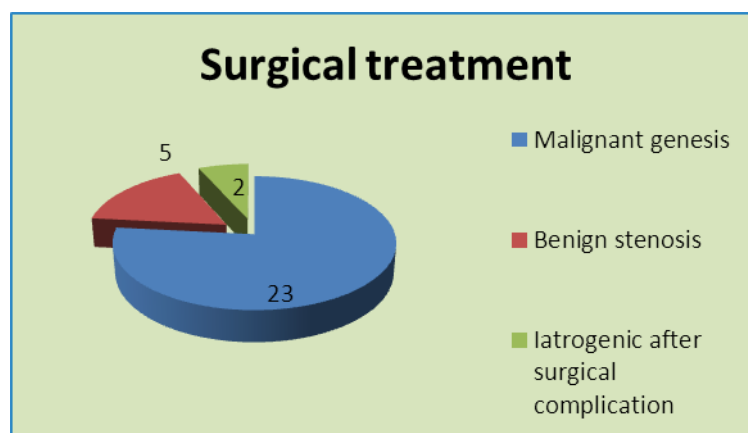


Fig. №39 Patients who underwent surgery (n=30)

In 23 of them, cannulation of the papilla of Vater was unsuccessful due to infiltration from the malignant process - 15 had pancreatic cancer, 5 - cholangiocarcinoma and 3 - metastatic lymph nodes compressing and/or infiltrating the common bile duct.

There were 5 patients with benign stenosis, the failure was due to the inability to cannulate the papilla of Vater and the common bile duct.

Two of the patients was with fully clipped common bile duct after cholecystectomy, contrast materia and guide did not move in the proximal direction, as a result of which stenting was not possible.

At the intrapancreatic/ampullary level, diagnostic/therapeutic ERCP was performed in 88 of 89 patients. One patient refused ERCP and was referred to other endoscopy centers. ERCP diagnosis coincided with the final one in 84 patients /95.5%/. The diagnostic possibilities are presented in fig40

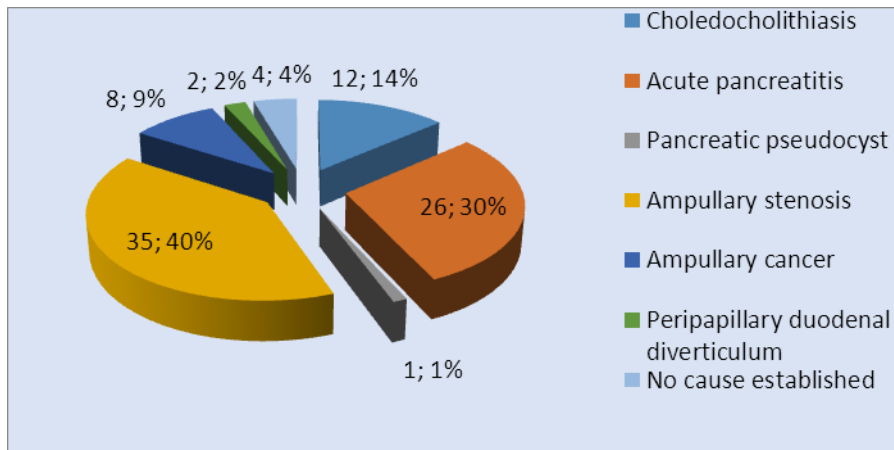


Fig.№40 ERCP possibilities at intrapancreatic/ampullary area (n=88)

About the localization of the cause of biliary obstruction in the intrapancreatic / ampullary area, we found:

-In 12 /13.6%/ patients who was diagnosed with choledocholithiasis, the concrements were located prepapillary. The papilla of the Vater was enlarged (bombed), the concrements were enclaved in the papilla, which did not allow cannulation. For therapeutic purposes, we used knife-type papillotomes to evacuate them. (Fig. № 41-42) Residual concrements were not found during the contrast of the bile ducts and the introduction of a balloon-extractor.

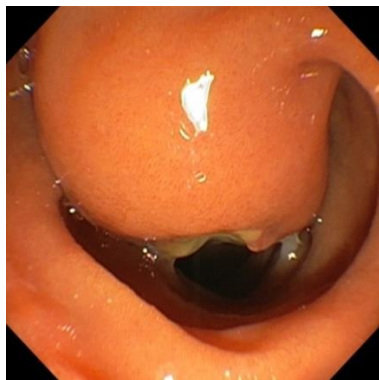


Fig.№ 41



Fig.№ 42

Bombed papilla of Vater and papillotomy

- In 35 /39.8%/ of the patients with a definitive diagnosis of sclerosing papilloiditis, the papilla of Vater was small, sclerotic. An endoscopic papillotomy was performed. No concrements or strictures were found after contrasting the bile ducts. (Fig. № 43,44) A balloon-extractor was introduced repeatedly, during which no concrements were evacuated, but stagnant bile contents. After the manipulation we observed clinical improvement and normalization of the laboratory parameters of the patients. Dilated intra- and extrahepatic bile ducts were not visualized after control abdominal ultrasound.

In four /4.6%/ patients, after contrasting the bile ducts in the distal third of the common bile duct, round shadows were visualized which were reported as concrements. The stones were not evacuated after papillosphincterotomy and repeated balloon extraction. In the control contrasting of the common bile duct, no defects in the filling were visualized.



Fig.№ 43
Fig.№ 44
Papillosphincterotomy in sclerosing papillooditis

- 2 /2.3%/ of the patients had peripapillary diverticulum. Papilla of Vater was located in the middle of two diverticulums. When the bile ducts were contrasted, a narrowing with smooth outlines in the distal third of the common bile duct was visualized. Papillosphincterotomy was performed on both patients and a plastic stent was placed. (Fig.№ 45,46)

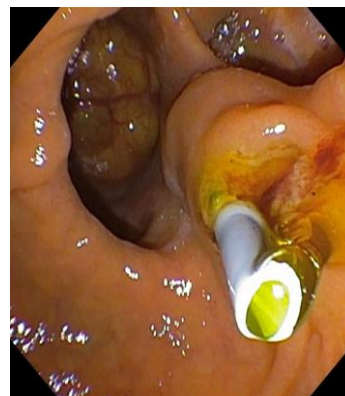
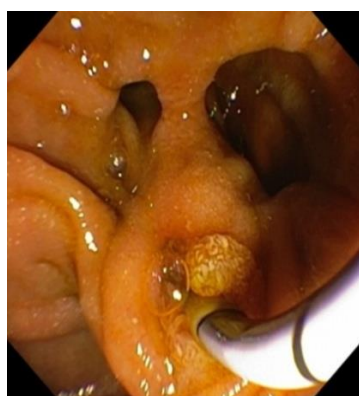


Fig.№45
Fig.№46
Compression from peripapillary diverticulum

- In 8 /9.1%/ patients the endoscopic diagnosis was papilla of Vater cancer. The latter had a rugged surface, reduced resistance of the overlying mucosa and a soft easily torn consistence. Histological material was taken from all patients and the diagnosis was confirmed. We performed prosthetics on the common bile duct - in seven patients a self-expanding metal stent / SEMS / 6 cm long - 10 mm lumen was inserted, in one - plastic 5 cm 10f. (fig.№ 47, 48, 49, 50)

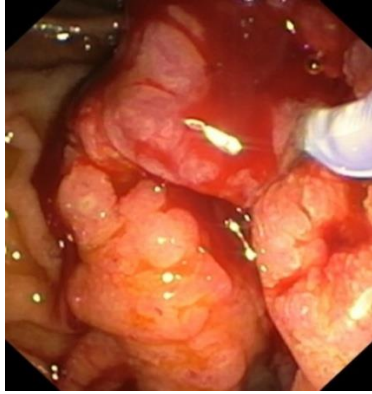


Fig.№ 47



Fig.№ 48



Fig.№ 49 Plastic stent

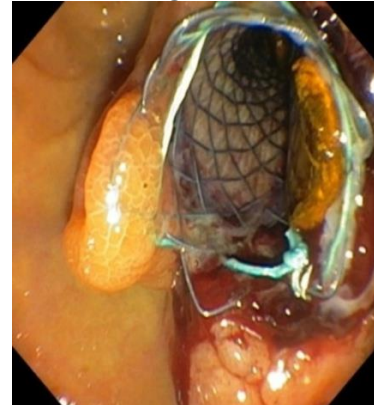


Fig.№ 50 Metal stent

- In 1 /1.1%/ patient with a definitive diagnosis of pseudocyst of the pancreas, narrowing with smooth outlines was visualized when contrastin the distal third of the common bile duct. Findings from imaging techniques and ERCP gave reason to think of compression by a pseudocyst of the pancreas. Two stents were inserted, SEMS in the common bile duct for bile drainage and plastic stent in the pancreatic duct for drainage of pancreatic juice; (Fig. №51)

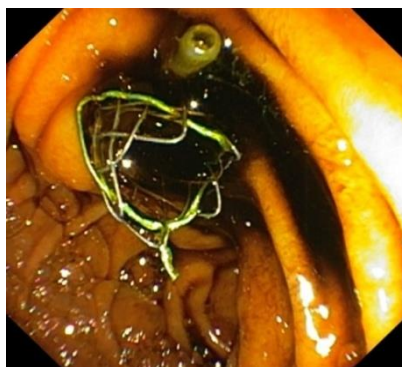


Fig.№ 51 SEMS and a plastic stent

- In 26 / 29.5% / patients with a definitive diagnosis of acute pancreatitis, after contrasting dilated bile ducts were found in 23 patients without defects in filling, and in 3 bile ducts were normal. Patients had laboratory, ultrasound, and CAT

data for acute pancreatitis. We performed a papillosphincterotomy to provide drainage of both bile and pancreatic juice to alleviate the pancreas.

We compared the average value of amylase on admission of patients at 6 hours, 24 hours and 48 hours after papillosphincterotomy. (tab.№9)

Patients number	26	26	19	8
Amylase	On Admission	6 hours after the papillosphincterotomy	24 hours after the papillosphincterotomy	48 hours after the papillosphincterotomy
Average value	1897.9	295.5	283.3	198.4
SD	173.5	374.5	401.3	206.8

Tab. № 9

It is clear from the table that the value of amylase after manipulation shows a decreasing trend.

The established sensitivity of ERCP at the intrapancreatic/ampullary level for the detection of extrahepatic cholestasis is 96.6%, the specificity -95.5%.

A definitive ERCP diagnosis of extrahepatic cholestasis with dilated intrahepatic bile ducts and common bile duct of various etiologies was found in 272 of 279 patients. The diagnostic value / sensitivity / for detecting obstructive jaundice is /97.5%/. The exact etiological cause during ERCP was established in 267 patients. The specificity is 95.7%.

The most common finding in diagnostic/therapeutic ERCP was choledocholithiasis in 130 /46.9%/ of 279 patients. The findings were: (Fig. №52)

- ✚ Choledocholithiasis - 130 /46,6%/;
- ✚ malignant obstruction - 74 /26,5%/;
- ✚ sclerotic papillooditis - 39 /14 %/;
- ✚ pancreatitis - 26 /9,3%/;
- ✚ compression of the common bile duct - 3 /1,1%/;
- ✚ compression of the common hepatic duct - 1 /0,4%/;
- ✚ postoperative stenosis - 6 /2,1%/.

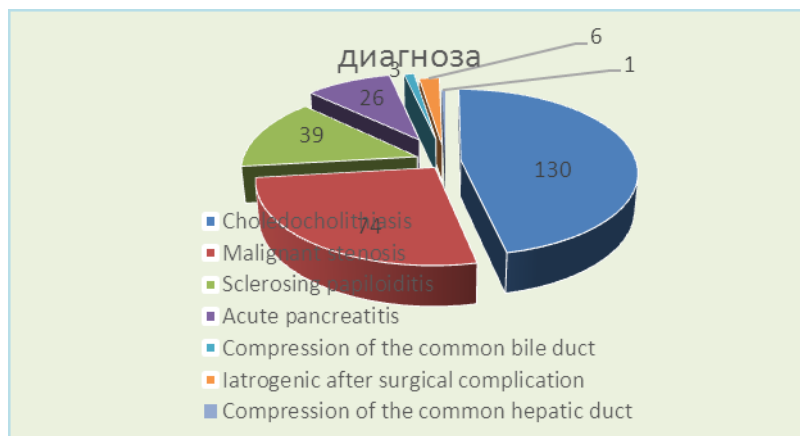


Fig. №52 Diagnosis established by ERCP (n=279)

In the group of malignant diseases the most common was pancreatic cancer - 39/14%/ patients, followed by cholangiocarcinoma - in 12 /4.3%/ patients. Klatskin tumor - in 10 /3.6%/ patients, papilla of Vater cancer in 8 /2.9%/ patients and gallbladder cancer - in 5 /1.8%/ patients.

5. Analysis of the causes, frequency and severity of complications in ERCP.

Due to the invasive nature of ERCP and the therapeutic manipulations, complications are inevitable. From 307 ERCPs of patients with extrahepatic cholestasis conducted in our study, complications were observed in 28 patients /9.1%/ -13 /46.4%/ men and 15 /53.6%/ women. There were more complications in patients over 60 years of age, with no significant difference between men and women. The most common complications of ERCP are presented in figure №53.

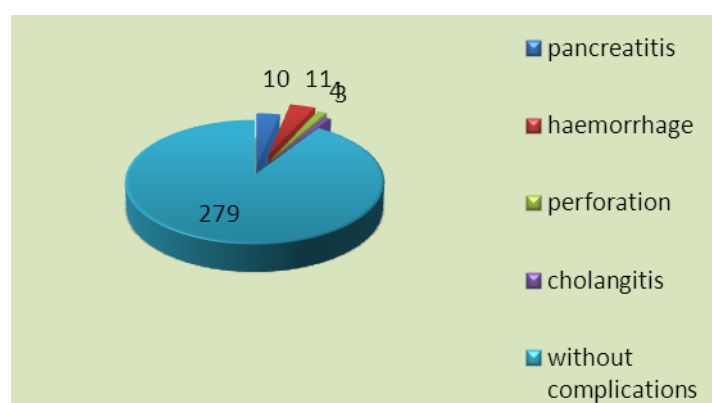


Fig.№53 Complications of ERCP (n=307)

- haemorrhage - in 11 /3,6%/ patients;
- pancreatitis - in 10 /3,3%/ patients;
- perforation - in 4 /1,3%/ patients;

➤ cholangitis - in 3 /1%/ patients.

The results obtained by us for the frequency of complications in ERCP correspond to the results published by most authors in the periodical literature.

5.1. Haemorrhage

From all the 307 patients who underwent ERCP, bleeding occurred in 11 /3.6%/ of them. From these - 6 /54.5% / men and 5 /45.5% / women, age ranged 20 - 77 years, with an average age of 57.63.

Only one patient had a low prothrombin time of 52.8% and a high INR-1.83, and the other 10 patients had normal coagulation status values.

The main cause of bleeding during and after ERCP is papillosphincterotomy. In all patients, bleeding occurred during the endoscopy. (Fig. № 54-55) We did not observe late bleeding. We classified it as clinically insignificant with clear blood sangvination during the manipulation. No decrease in hemoglobin of more than 3 units was observed, which did not require hemotransfusion.

In 7 patients the bleeding stopped spontaneously until the end of the study. In the other 4 patients, in whom the hemorrhage apparently persisted, endoscopic injection hemostasis was applied - Adrenaline solution 1: 10000, on the outer part of the upper edges of the incision. The drug substance was injected submucosally using an endoscopic injector to achieve a combined effect of vasospasm and local tamponade. Patients were actively monitored and conservative therapy with hemostatics and PPIs was performed. Surgical treatment was not performed in these patients.

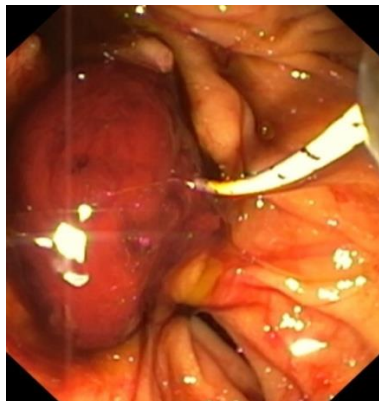


Fig.№ 54

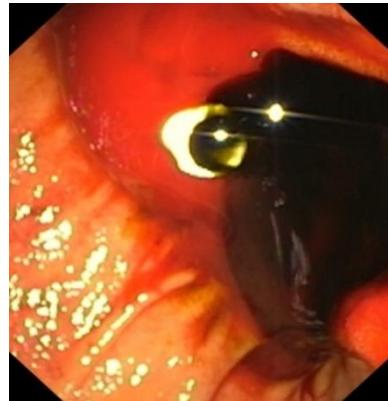


Fig.№ 55

Bleeding after papillosphincterotomy

5.2. Hyperamylasemia and PEP.

High amylase levels at 6 hours post-manipulation compared to baseline levels were found in 72 /23.4%/ of all 307 patients. The patients were mostly women /70.9%/, men /29.1%/. After 24 hours, there was a tendency of decreasing and normalizing amylase in 62 /86,1%/ patients. Patients had no clinical data of PEP.

In 10 /3.3%/ patients we observed post-ERCP pancreatitis / PEP / with several-fold increase in the value of amylase compared to baseline levels and manifestation of abdominal pain 24 hours after the procedure - 4/40%/ were men and 6/60 %/ - women. The age ranged from 37 to 80 years. The reason was papillosphincterotomy and contrast of the pancreatic duct.

The dynamics of amylase after ERCP is presented in Fig. №56

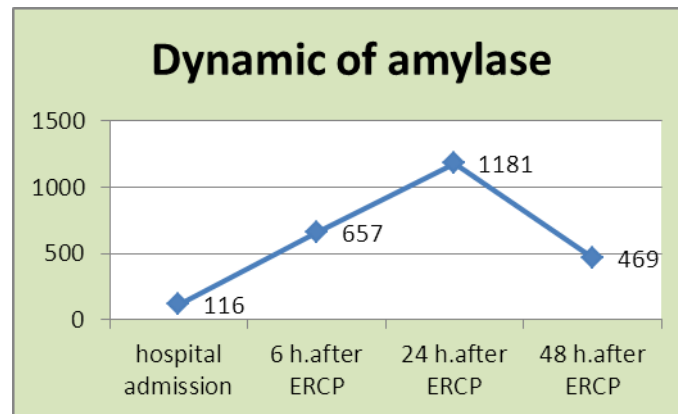


Fig. №56 Dynamic of amylase in ERCP (n=10)

Patients diagnosed with PEP were:

- 7 patients with choledocholithiasis;
- 3 patients with malignant stenosis of the common bile duct.

The severity of pancreatitis was defined according to the classification of Cotton et al.:

- mild PEP - 5 patients with elevated amylase levels up to 3 times above the measured baseline levels 24 hours after ERCP. The hospital stay was extended by an average of 2 days;

- moderate PEP - 2 patients, amylase levels 5 times above baseline. Hospital stay was extended by an average of 8 days;

- severe PEP - with significantly higher amylase levels. The patients were in damaged condition and the hospital stay was extended by more than 10 days. They underwent surgery which detected hemorrhages and steatonecrosis in the gland. There was no lethal outcome in PEP.

5.3. Cholangitis

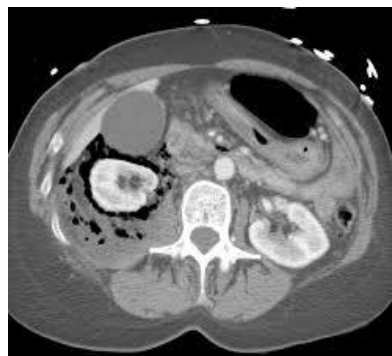
We observed clinical manifestations of cholangitis after ERCP in 3 patients /1%/, of which 1 man and 2 women over 77 years of age. Subfebrile fever, shaking, and biochemical constellation for inflammation of the bile ducts with elevations in cholestasis enzymes, leukocyte number, bilirubin, and CRP were found after the manipulation.

Two of them had choledocholithiasis and one had stenosis of the distal part of the common bile duct from a tumor of the head of the pancreas with a plastic stent placed.

We continued the therapy with infusions of aqueous-saline solutions, antispasmodics, antibiotics and antipyretics. Due to the persistence of the complaints and the biochemical constellation, using non-invasive instrumental studies we proved incomplete drainage of the bile ducts - stent occlusion in one patient and the presence of residual stones in two patients. We performed ERCP again, the occluded stent was replaced, and after revision of the common bile duct, the stones were removed and a plastic stent was preventively placed.

5.4. Perforation

From 307 ERCPs performed with papillosphincterotomy we made perforation in 4 patients /2 men and 2 women in the age range 54-80 years/. Frequency - 1.3%. Choledocholithiasis was diagnosed in 3 patients and sclerosing papilloiditis in 1 patient. The perforation was retroperitoneal and was not detected during the invasive procedure. After waking up the patients from anesthesia due to clinical data for acute abdomen, a native abdominal X-ray and CAT was performed, in which free gas was found retroperitoneally and in the abdominal cavity (fig. № 57, 58). One patient had subcutaneous emphysema and was diagnosed with pneumothorax. Patients were consulted with a surgeon and operated.



Фиг.№ 57



Фиг.№ 58

CAT free gas data in abdomen

5.5. Complications of stenting the common bile duct

Prosthesis dysfunction was found in 11 /13.4%/ of 82 patients:

- It had migrated distally /into the duodenum/ in one patient - it was removed and a new plastic stent was placed.
- We found proximal migration in one patient, which required withdrawal of the stent in the distal direction. (Fig.№ 59)
- In 9 patients, occlusion was found from biofilm formation (due to increased viscosity of bile juice) on the inner surface, leading to lumen obstruction. From them:
 - In 4 patients 8-12 months after placement of a self-expanding metal stent - we recanalized the stent with saline and a balloon. (Fig.№ 60)
 - In 5 patients, 2-5 months after implantation of a plastic stent - the stent was replaced with a new plastic one.

To prolong the functional time of the stents, we administered drugs containing ursodeoxycholic acid for an extended period of time.



Fig.№ 59 Migrated plastic stent

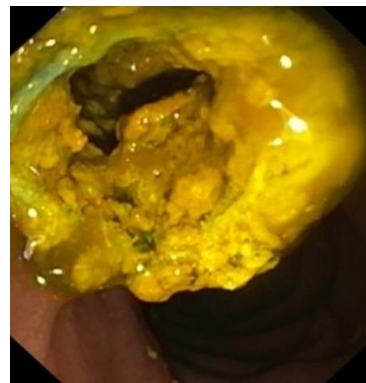
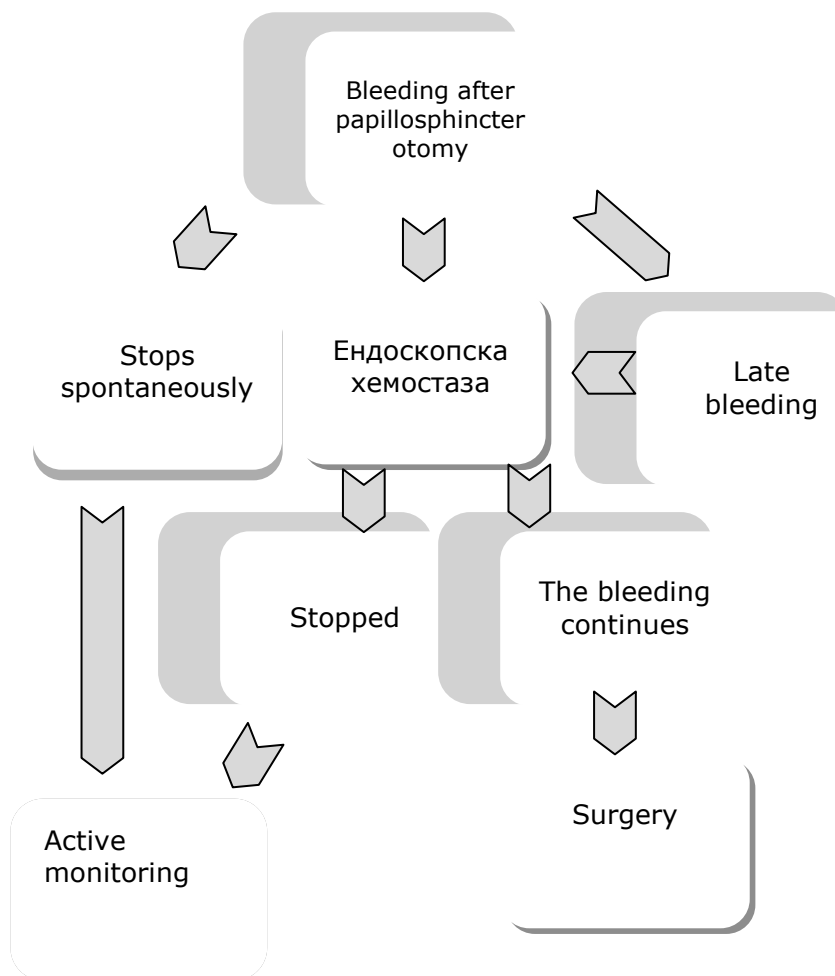


Fig.№ 60 SEMS occlusion

6. Diagnostic-therapeutic algorithm of behavior in case of complications of ERCP.

The presented study, based on literature data and own results, allowed us to offer an optimized approach for diagnostic and therapeutic behavior in the event of complications after ERCP. The results of our scientific work proves that this strategy is effective. We think that the proposed algorithms are beneficial for the wider professional community.

6.1. Algorithm of behavior in post-ERCP bleeding

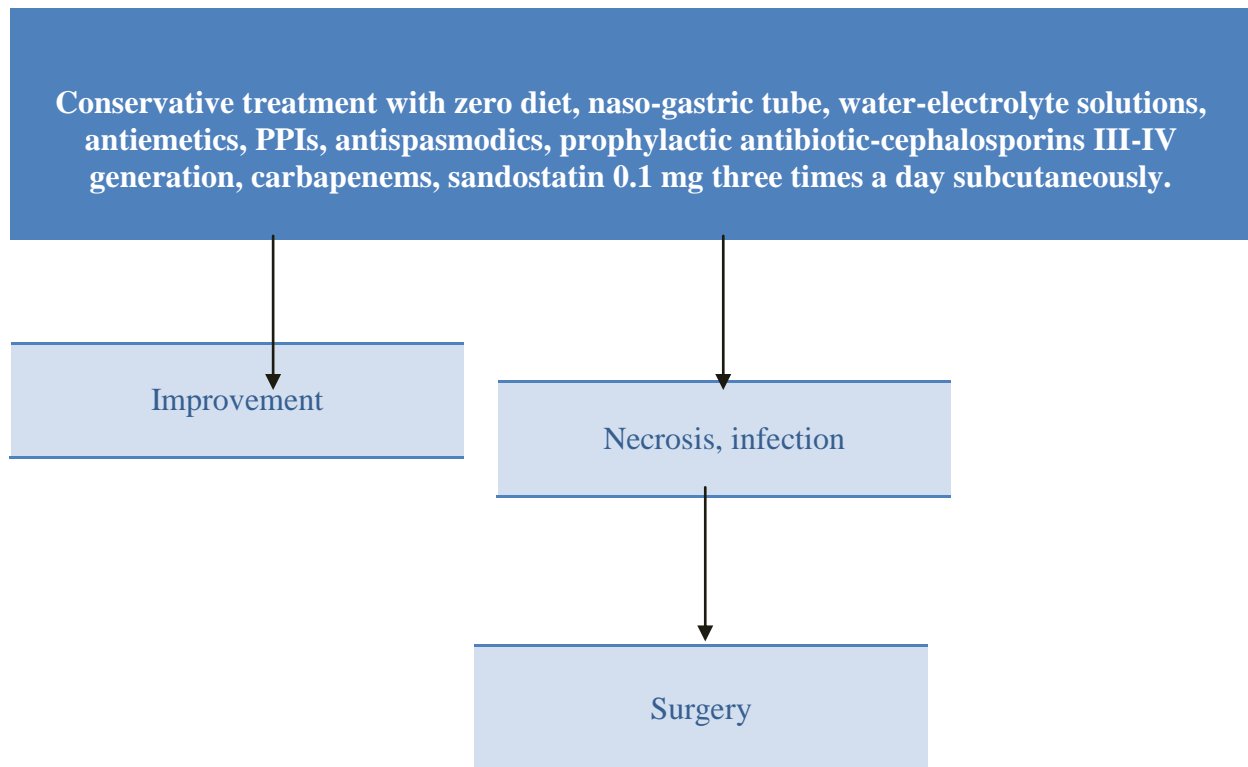


Bleeding after papillosphincterotomy is usually mild and stops spontaneously. In some cases, endoscopic injection therapy with adrenaline solution, placement of blood clips and thermal hemostasis are required. In a few of the cases, bleeding was manifestive, requiring blood transfusion and surgical treatment.

6.2. Pancreatitis.

PEP is thought of as new or persistent abdominal pain, an increase in serum amylase levels 3 or more times above the normal value measured after the 24th hour of the procedure.

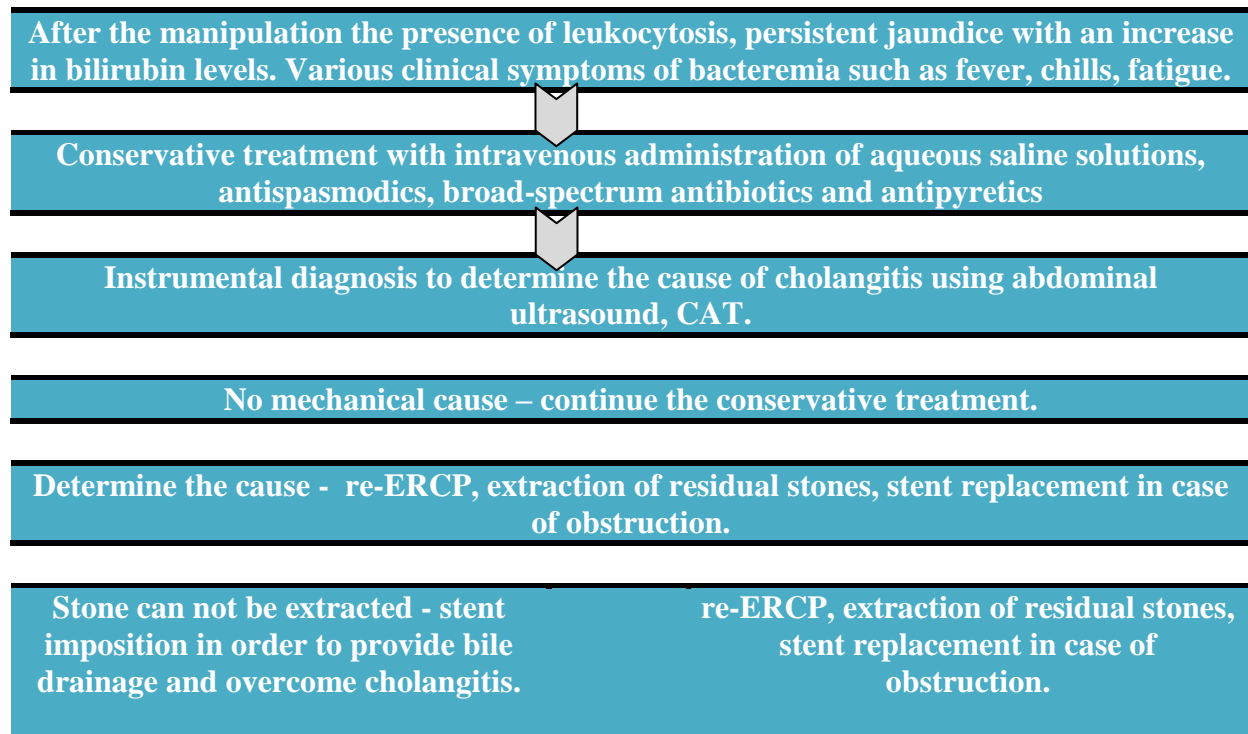
Algorithm of behavior in PEP



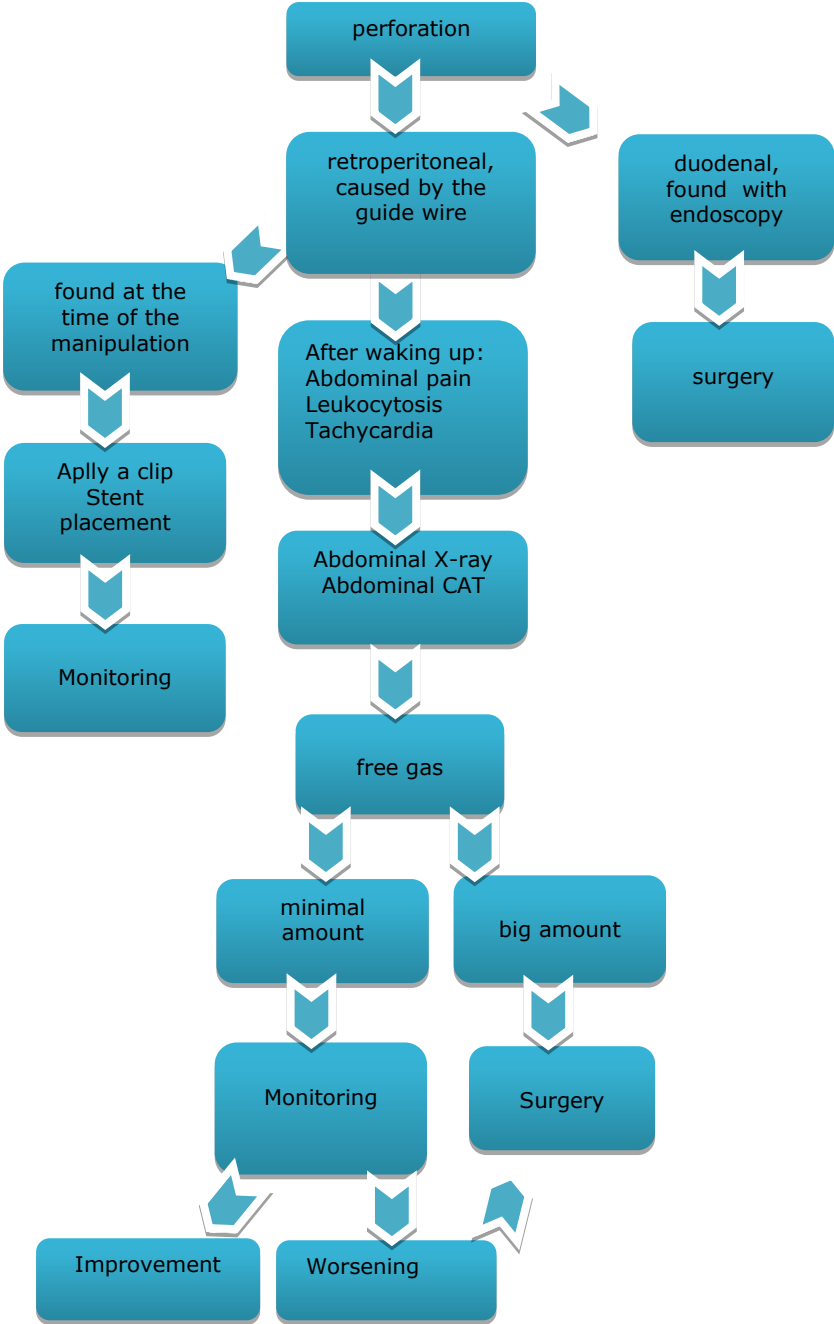
6.3. Cholangitis

It occurs in infected bile and impaired drainage of bile. Septicemia and bacteremia may occur after ERCP in patients with stones or stenosis who have not achieved adequate bile drainage and in patients with obstructed biliary stents.

Algorithm of behavior in post-ERCP cholangitis



6.4. Algorithm of behavior in post-ERCP perforation



Presence of minimal amount of gas retroperitoneally found by CAT without clinical data for perforation– monitoring.

7. DISCUSSION

Extrahepatic cholestasis occupies an important place in clinical practice. It is a syndrome involving benign and malignant diseases leading to impaired drainage of bile. Despite advances in diagnosis and therapy, the incidence remains high worldwide, including in our country. Dealing with the obstructive jaundice is a main problem in emergency medicine, it requires prompt intervention by a multidisciplinary team.

The treatment of patients with extrahepatic cholestasis is stepwise. The first step is to assess the clinical condition and biochemical parameters. It is followed by performing non-invasive instrumental methods - abdominal ultrasound and, if necessary, computed tomography and magnetic resonance cholangiography. They do not always manage to accurately diagnose the pathology, which requires invasive diagnostics with ERCP. It is performed as a diagnostic method to confirm the finding that led to biliary obstruction and a subsequent therapeutic method. ERCP compared to other standard gastrointestinal procedures is technically far more difficult, requiring more skills.

After contrasting the bile ducts, it manages to diagnose the cause of the obstruction and remove it in most of the cases. Therapeutic behavior includes performing a papillosphincterotomy, in cases of stenotic papilloiditis, stones extraction from the common bile duct, and stent placement in the presence of strictures/stenosis to provide bile drainage. Endoscopic treatment allows non-surgical resolution of mechanical jaundice in 85-90% of the cases [123]. We performed ERCP in 307 patients included in our study, the success rate was 90.9%.

According to ESGE, complete removal of the concrements should be $\leq 90\%$ [123]. We found stones in the common bile duct in 130 patients. We successfully evacuated them in 128 /98.5%/ patients, using a balloon-extractor and a Dormia basket. The extraction of large casting stones over 25-30 mm was unsuccessful. In two patients, we placed a temporary plastic stent passing over the stones, to provide drainage and control the underlying cholangitis. The placement of temporary stents is also recommended by ESGE. Studies show that most of the stones decrease in size [131]. These cases are indicated for re-ERCP with choledochoscopy and lithotripsy.

Endoscopic bile duct stenting is a widely used method for palliative treatment of malignant obstructions and for treatment of benign biliary tract diseases such as biliary fistulas and strictures. The selection of an appropriate stent is performed according to strictly defined criteria according to the consensus of ESGE. In 84 /30.1%/ patients, we controlled the extrahepatic cholestasis by placement of plastic and self-expanding metal stents. The choice of stent was made according to the consensus of ESGE and the financial capabilities of the patients.

In malignant biliary strictures, endoscopic stent placement is associated with better survival, faster recovery, low complication rates, and significantly better quality of life compared to palliative surgery [226, 309].

In the examined group of 307 patients we observed complications in 28 /9.1%/ patients. PEP was observed in 10 /3.3%/, hemorrhage in 11 /3.6%/, perforation in 4 /1.3%/ and cholangitis in 3 patients /1%/. The data on the frequency of complications after ERCP are comparable with the data from the literature discussed in the review [55, 100, 123, 137, 145].

To prevent PEP, the ESGE and ASGE consensus suggest the use of NSAIDs rectally in patients who will undergo ERCP [67, 128, 133]. In our study of 55 patients hospitalized in the GED for ERCP, we investigated the effect of drug prophylaxis. In 30 patients we used NSAIDs (Profenid) administered rectally in the morning, before and after the procedure. Patients were randomly selected without regard to gender, age and admission diagnosis

All patients were monitored clinically and laboratory for pancreatitis after the procedure. None of them had data on PEP. From the patients in whom no prophylaxis was performed, three had clinical and laboratory evidence of PEP after ERCP. Their hospital stay was extended. Our observations showed that the use of profenid suppositories prevents PEP and significantly improves the clinical condition of patients. Although a small group, our data are comparable with the data from the literature on drug prophylaxis [67, 121, 123, 128, 133].

The mortality rate after therapeutic ERCP in our study was 0.9%, and it was due to complications after perforation. Our frequency is higher than reported in other studies, where it is reported to be 0.4% - 0.5% [55, 230].

The diagnostic possibilities of the non-invasive imaging methods and ERCP in extrahepatic cholestasis are presented in fig. 61

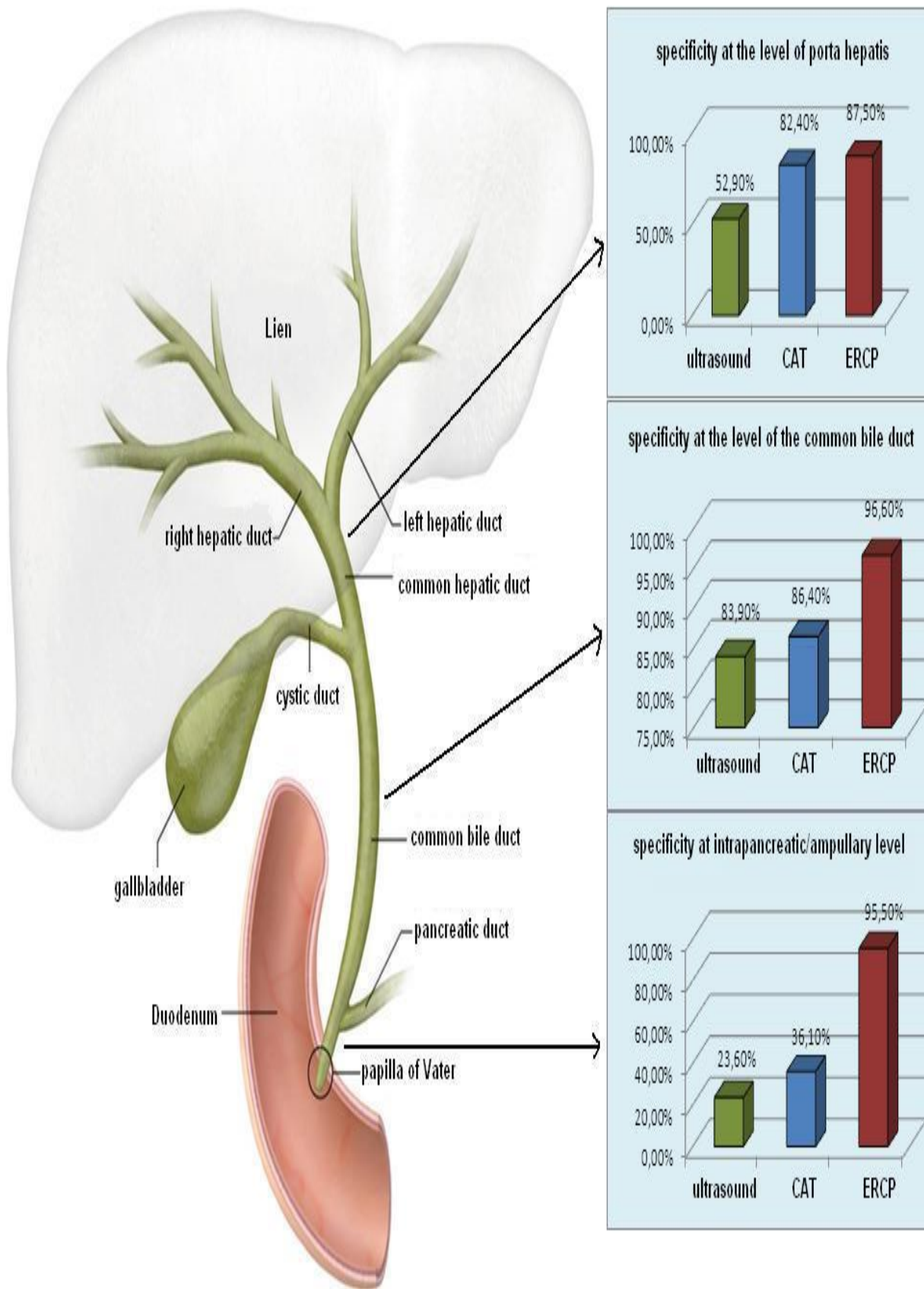


Fig.№ 61 Diagnostic possibilities of imaging methods in extrahepatic cholestasis

It can be seen from the figure that non-invasive instrumental methods have a high diagnostic value for establishing the exact cause of extrahepatic cholestasis when the process is localized at the level of the common bile duct. In other localizations the values are limited. ERCP has a high diagnostic value at all levels of extrahepatic cholestasis. The obtained results confirm the high efficiency and indisputable advantages of the invasive endoscopic procedure and the need for its implementation. It allows definitive treatment of a number of diseases of the biliary tract and pancreas at the time of their diagnosis. The application of this method requires a multidisciplinary team of an experienced endoscopist, radiologist, anesthesiologist and surgeon.

8. Conclusion

Extrahepatic cholestasis is a syndrome involving diseases that occur with impaired drainage of bile. The problem is topical due to the increasing frequency of patients with mechanical jaundice irrespective of its cause, population aging and the need of prompt solution.

The present study discusses some very important for clinical practice guidelines for diagnosis with laboratory and non-invasive instrumental methods as a first stage and ERCPG as a diagnostic-therapeutic approach in extrahepatic cholestasis. The need for adequate diagnosis and treatment requires close cooperation and dialogue between specialists from the clinical laboratory, radiologists, gastroenterologists, surgeons and anesthesiologists. The multidisciplinary approach, the team work and the complete coordination between the individual units are essential for the timely and successful diagnosis and treatment.

The gastroenterologist-endoscopist with his knowledge and skills about performing endoscopic retrograde cholangiopancreatography is a key figure in controlling the mechanical jaundice. Therefore, we call for timely diagnosis, hospitalization and immediate endoscopic intervention

The main causes of obstructive jaundice are choledocholithiasis and malignancies of the head of the pancreas. In most cases, patients with malignancy are inoperable and the therapeutic behavior is palliative decompression of the bile ducts through placement of a plastic or a self-expanding metal stents.

Due to its invasive nature, ERCP is accompanied by complications. Prevention of complications during papillosphincterotomy can be achieved by applying effective prevention strategies and careful handling with the accessories during ERCP. Knowledge and prevention of the factors that provoke complications determine the success of treatment.

9. Inference:

1. The main instrumental diagnostic methods for establishing the level and etiological cause of extrahepatic cholestasis are abdominal ultrasound, CAT, MRC and ERCP;

2. The most common cause of extrahepatic cholestasis was choledocholithiasis in 42.4%, followed by malignancy in 31.5%. The average age of the patients was 68.24 years. In benign causes of extrahepatic cholestasis, the female sex prevailed /53.5%/, and in malignant diseases - the male sex /56.1%/;

3. The diagnostic possibilities of the instrumental methods by levels are: porta hepatis - abdominal ultrasound - 52.9%, CAT - 82.4%, ERCP - 87.5%, common bile duct - abdominal ultrasound - 83.9%, CAT- 86.4%, ERCP- 96.6%, intrapancreatic/ampullary area - abdominal ultrasound - 23.6%, CAT - 36.1%, ERCP - 95.5%;

4. The total diagnostic sensitivity is: abdominal ultrasound - 84%, CAT - 91.1%, ERCP - 99.5%, and the specificity - abdominal ultrasound - 65%, CAT - 65.5%, ERCP - 95.7%;

5. ERCP has a high diagnostic value for establishing the exact cause of extrahepatic cholestasis at all levels, when non-invasive instrumental methods - only in localization of the process at the level of the common bile duct.

6. The performance of ERCP allows definitive treatment in case of choledocholithiasis;

7. Repeated ERCP is a reasonable alternative in patients with clinical, laboratory and instrumental evidence of obstructive jaundice after incomplete extraction of stones from the common bile duct;

8. Performing papillosphincterotomy in patients with pancreatitis shows good results in controlling glandular edema in combination with conservative measures;

9. In malignant biliary strictures ERCP with stent placement is associated with faster recovery, low complication rate and significantly better quality of life compared to palliative surgery;

10. The frequency of complications during ERCP in patients with extrahepatic cholestasis is 9.1%, of which hemorrhage - 3.6%, pancreatitis - 3.3%, perforation 1.3% and cholangitis 1%. The lethality rate is 0.9%.

10. CONTRIBUTIONS

1. The etiology and epidemiology of extrahepatic cholestasis have been studied.
2. The general and depending on the place of obstruction diagnostic value of the non-invasive instrumental methods and ERCP in patients with extrahepatic cholestasis have been studied and analyzed.
3. The effectiveness of papillosphincterotomy in patients with acute pancreatitis to control glandular edema in combination with conservative measures has been confirmed.
4. The role and effectiveness of ERCP and papillosphincterotomy in the treatment of patients with choledocholithiasis have been confirmed.
5. The role of ERCP with stent placement has been proven as a first-line treatment for palliative therapy in malignancies.
6. The frequency of complications during ERCP in patients with extrahepatic cholestasis has been confirmed.
7. An optimized, clinically applicable algorithm for behavior in case of complications after ERCP has been proposed.

11. LIST OF THE PUBLICATIONS AND SCIENTIFIC COMMUNICATION RELATED TO THE DISSERTATION

1. **Sarafiloski G.**, I.Lalev, M.Vlahova, Z.Gorcheva, D.Stefanova, S.Iliev, E.Filipov, D.Stoykov, P.Marinova, Diagnostic and therapeutic capabilities of the endoscopic retrograde cholangiopancreatography in mechanical jaundice, First national congress of Young Gastroenterologists,27-28.03.2015, Sofia.
2. Stoykov D. , I. Lalev, S. Iliev, I.Dekova, M. Yanchev, P.Marinova, M. Vlahova, **G. Sarafiloski** Retroduodenal perforations-surgery treatment. XV national surgery congress with international participation. 29.09-.02.10.2016 Reports,pages.286-291.
3. L. Tsankov, N. Totsev, P.Stefanovski, S.Popovski, **G. Sarafiloski** - „A case of patient with clinical and radiological data for pneumoperitoneum after ERCP” – „Emergency medicine” magazine, 2016,20/1/,66-68
4. **Sarafiloski G.**, M. Vlahova, I.Lalev. Complications in endoscopic retrograde cholangiopancreatography. “Medical. Magazine“ magazine, 03.2018, number.51,page.102-104 .
5. D.Stoykov, I.Lalev, P.Marinova, I. Dekova, **G.Sarafiloski**. Methods and criteria for Diagnosis of diseases of the gallbladder and bile ducts. Differential diagnosis. IV Scientific-practical conference of Bulgarian asociation of medical doctors.. 26-29.04.2018. Nesebar. Reports.
6. **G. Sarafiloski**, M. Vlahova, I.Lalev. Endoscopic retrograde cholangiopancreatography in choledocholithiasis. Acute abdomen. Expertise in surgical cases reaching medical jurisprudence. National Conference on Surgery, 05-07.06.2019. Pleven. Reports.
7. M. Vlahova, **G. Sarafiloski**, I.Lalev. Role of ultrasound in the diagnostic algorithm of ASA. Acute abdomen. Expertise in surgical cases reaching medical jurisprudence. National Conference on Surgery, 05-07.06.2019. Pleven. Reports.
8. **Sarafiloski G.**, Vlahova M. Complications of invasive endoscopic procedures on the hepatobiliary tract. Oral presentations. Abstracts from Jubilee Scientific Conference “45 years Medical University – Pleven”, 31.10-02.11, 2019, Pleven. J Biomed Clin Res Volume 12, Number 1, Supplement 2, 2019.
9. **Sarafiloski G.**, Vlahova M., Biliary stents in inoperable pancreatic cancer. Posters. Abstracts from Jubilee Scientific Conference “45 years Medical University – Pleven”, 31.10-02.11, 2019, Pleven. J Biomed Clin Res Volume 12, Number 1, Supplement 2, 2019.
10. Yanchev M., Sabotinov Ts., Dekova I., **Sarafiloski G.**, Vlahova M., Tonchev P., Stoykov D., Surgery for Mechanical Jaundice after Unsuccessful Endoscopic Treatment. Posters. Abstracts from Jubilee Scientific Conference “45 years Medical University – Pleven”, 31.10-02.11, 2019, Pleven. J Biomed Clin Res Volume 12, Number 1, Supplement 2, 2019.