ORIGINAL ARTICLE

CONTENTS

Small common bile duct – the risk factor for post-ERCP pancreatitis in patients with choledocholithiasis

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ABSTRACT

Aim: To investigate the risk factors for PEP in patients with choledocholithiasis

Materials and Methods: We have retrospectively analyzed 253 cases with choledocholithiasis that underwent ERCP. The primary endpoint was the occurrence of PEP. A number of potential risk factors for PEP were taken into account: gender, age (10 mm); type of choledocholithiasis – microcholedocholithiasis, choledocholithiasis (1-2 stones), multiple choledocholithiasis (≥ 3 stones) and choledocholithiasis due to Mirizzi syndrome; periampullary diverticulum; papilla size (≤5 or >6 mm); ERCP success; selective biliary cannulation; pancreatic cannulation/injection; precut; papillotomy.

Results: PEP was in 8 (3,2 %) cases. Univariate analysis identified two factors associated with PEP – common bile duct ≤10 mm (P=0.045) and papilla ≤5 mm (P=0.036). In multivariate analysis, among all variables only the common bile size ≤10 mm appeared to be significant (P=0.018).

Conclusions: In patients with choledocholithiasis the occurrence of PEP is related to common bile duct size less than 10 mm.

KEY WORDS: risk factor, ERCP, choledocholithiasis, post-ERCP pancreatitis

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is an invaluable procedure in the diagnosis and management of pancreaticobiliary disorders. Most often ERCP treatment modalities are used in biliary diseases such as common bile duct stones or malignant biliary obstruction. In case of common bile duct stone ERCP is a routine and primary method to be used. The stone removal rate and ranges from 74% to 98% and usually is higher than 90 % [1]. Among patients who undergone ERCP common bile duct stone is the indication for it in majority of cases – 50-70 % [2-5].

Nevertheless, the incidence of adverse events reported after ERCP is between 4 and 20% [2 ,4,5,]. Post-ERCP pancreatitis (PEP) is the most common and serious complication after ERCP and related endoscopic procedures [2, 4-7]. The incidence of PEP was reported to be 1% to 19,6% [2, 3, 8]. Being a serious complication PEP extends the hospital stay and increases hospital costs, and in severe cases may even lead to fatal outcome [6, 7].

In general PEP risk factors have been well investigated [2-17], identification of these factors is essential to the recognition high-risk cases in which ERCP should be avoided if possible, or in which protective measures should be done [6-8, 10, 14]. Factors are generally divided into two groups: patient-related factors and procedure-related factors.

Despite the plenty of works discovering the PEP risk factors, these factors vary from work to work. The reason for this may be in differences of patients' groups and indications for ERCP, operator preference and experience and other factors.

AIM

The aim of this study was to investigate the risk factors for PEP in patients with choledocholithiasis as the most common indication for ERCP.

MATERIALS AND METHODS

PATIENTS

We retrospectively analyzed the records of patients (form № 003/o) of all consecutive cases with undergo-

ing ERCP between January 2013 and December 2020. Indications for ERCP were determined on the basis of clinical and radiologic finding. There were 355 patients with choledocholithiasis (Fig.. 1). Exclusion criteria were: papillotomy in history, complications (biliary pancreatitis and/or cholangitis), ampulla impacted sone, Billroth II gastrectomy and incomplete medical data (lack of laboratory and visualisation data after ERCP).

ERCP

ERCP was performed by two experienced operators (K.O. Kramarenko, I.M. Mamontov). Before the procedure all patients received diclofenac (100 mg) per rectum for PEP prevention [18]. Premedicated with an injection of scopolamine butylbromide (10–20 mg) and local anesthesia of the pharynx with 8 % lidocaine were done.

Procedure usually was started with a guided sphincterotom or canula. Priority was given to obtain selective biliary cannulation which is defined as deep canulation of common bile duct through naïve papilla followed by cholangiography without canulation of pancreatic duct or wirsungography. Precut papillotomy was used to achieve biliary access in case of failure of selective biliary cannulation after 5-10 attempts or approximately 5 min of trying. After cholangiography and estimating quantity and size of the common bile duct stone sphincterotomy and lithoextraction with basket were done. In case of need mechanical lithotripcy was used. Ballon dilatation was used only after sphincterotomy in case of distal common bile duct and/or its orifice was much smaller than the stone. Maximum balloon size was 12 mm. If complete removal was not achieved, nasobiliary drainage or biliary stenting was considered.

After the procedure, the patient fasted until the next morning, received an intravenous infusion and ceftriaxone (2 g). Blood tests – hemoglobin, bilirubin and amylase levels were measured at baseline, 4-8 hours after the procedure, and next morning. Biliary decompression was confirmed by decreasing bilirubin level and common bile duct size which was measured by ultrasound. ERCP-related adverse events and incidents were recorded. PEP was defined as upper abdominal pain with amylase levels more than three times the normal rate [18]. The severity of PEP was defined as mild (no organ failure, no local or systemic complications); moderate (transient organ failure, local or systemic complications without persistent organ failure); severe (persistent organ failure) [18].

The primary endpoint of this study was the occurrence of PEP in patients with choledocholithiasis. Although some of the studied patients, who had more than 1 ERCP procedure performed, PEP incidence was analysed only after the first session. A number of potential risk factors for PEP were analysed. All variables were made as categorical and included: gender, age (< 60 or ≥ 60 years); blood total bilirubin level (normal or increased); common bile duct size (≤10 or >10 mm); type of choledocholithiasis – microcholedocholithiasis, choledocholithiasis (1-2 stones), multiple choledocholithiasis (≥ 3 stones) and choledocholithiasis due to Mirizzi syndrome; periampullary diverticulum; papilla size (≤5 or >6 mm); ERCP success; selective biliary cannulation; pancreatic cannulation/injection; precut; papillotomy.

STATISTICS

To detect the association between PEP and any categorical variable univariate analyse was performed by Chi-square test (χ^2). Also, all variables were taken for entry into multivariate analyses by multinominal regression. A P-value less than 0.05 was regarded as significant. Variables with P<0,05 both for univariate and for multivariate models considered as a PEP risk factor.

Statistical analysis was done with SPSS® version 19 (IBM, USA).

RESULTS

Characteristics and medical data of the patients are presented in Table 1

Two-thirds of the patients were female (66%) and 17,8% of patients had cholecystectomy in history. The main clinical sign was jaundice. Initial ERCP was achieved in 98 % cases and complete stone extraction in 90,5 %.

Among 8 patients with PEP mild pancreatitis was in 6 cases, moderate – in 1 and severe in 1 patient. There was no lethal outcome. In case of more than 1 ERCP procedure/session needed there were no cases of PEP after the 2nd or 3d session.

Table 2 shows the results of univariable and multivariable analyses with the endpoint of PEP.

Univariate analysis (Table 2) identified two factors associated with PEP – common bile duct ≤10 mm (P=0.045) and papilla ≤5 mm (P=0.036).

In multivariate analysis (Table 2), among all variables only the common bile size ≤10 mm appeared to be significant (P=0.018). Other variables including the papilla size were not significant (P>0,05).

DISCUSSION

ERCP is a well-known preferred procedure for treating choledocholithiasis with a highly successful rate and relative safety [1, 6, 7]. Common bile duct stones are

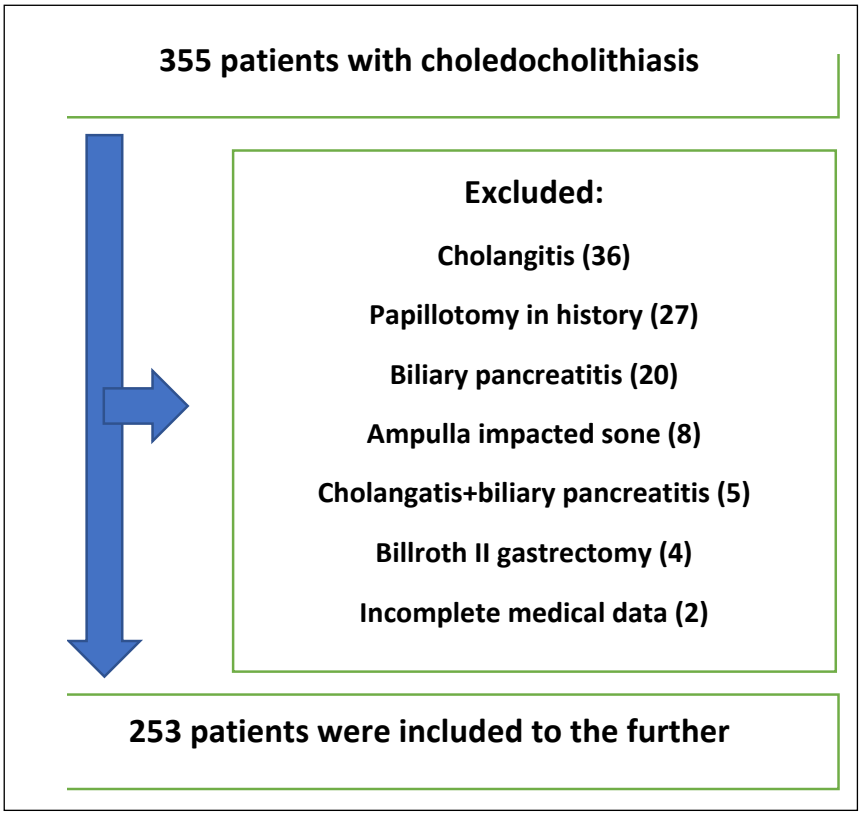

Fig. 1. Inclusion flowchart of the study.

Table 1. Baseline and Clinical Characteristics of the Patients with Choledocholithiasis (n=253)

Measure	Value
Age (range), yrs	64±14,6 (20-91)
Male/Female	86/167
History of cholecystectomy	45 (17,8 %)
Total bilirubin level (range), mmoll/l	71±61,2 (10-426)
Common bile duct (range), mm	12±3,8 (4-28)
Type of common bile duct stones	
Microcholedocholithiasis	38 (15 %)
Choledocholithiasis (1-2 stones)	166 (65,1 %)
Multiple common bile duct stones (≥3)	35 (13,8 %)
Common bile duct stone(s) due to syndrome Mirizzi	14 (5,5 %)
Periampullary diverticulum	44 (17,4 %)
Initial ERCP success	248 (98 %)
Selective biliary cannulation	190 (75,1%)
Pancreatic cannulation/injection	33 (13%)
EPST	231 (91,3 %)
Precut	73 (28,9 %)
Balloon dilatation of common bile duct	2 (0,8 %)
Complete stone extraction	229 (90,5 %)
> 1 endoscopic session required	52 (20,6 %)
PEP	8 (3,2 %)

the most common indication for ERCP [2-5]. However, despite improvement of the equipment for ERCP and implemented options for PEP-preventing in recent years, the incidence of PEP has not decreased significantly [4, 10]. In case when ERCP is considered to be used, identifying high risk patients for PEP is crucial for choosing treatment strategy and prevention measures [10, 12-14].

Table 2. Univariate and multivariate analysis of risk factors for PEP

Variables	PEP	Non -PEP	Analysis					
			Univariate		Multivariate			
			χ^2	P	B	P	Exp (B)	CI (95%)
Gender								
Male	5	81	2.992	0.084	0.580	0.509	1.787	0.320 - 9.990
Female	3	164						
Age, years								
< 60	3	64	0.515	0.473	1.344	0.189	3.835	0.515 - 28.559
≥ 60	5	181						
Blood bilirubin level								
Normal	0	48	1.934	0.164	-*	-*	-*	-*
Increased	8	197						
Common bile duct, mm								
≤10	6	97	4.024	0.045	2.539	0.018	12.665	1.539 - 104.196
>10	2	148						
Type of choledocholithiasis								
Microcholedocholithiasis	1	37						
Choledocholithiasis (1-2 stones)	6	159	2.016	0.570	-*	0.694	-*	-*
multiple choledocholithiasis (≥ 3 stones)	0	35						
Mirizzi syndrome	1	13						
Periampullary diverticulum								
Yes	3	41	2.325	0.127	2.044	0.056	7.718	0.952 - 62.542
No	5	204						
Papilla size, mm								
≤5	2	15	4.405	0.036	2.928	0.124	7.601	0.572 - 101.072
>6	6	230						
ERCP success								
Yes	8	240	0.167	0.683	-*	-*	-*	-*
No	0	5						
Selective biliary cannulation								
Yes	6	184	0.000	0.995	1.617	0.309	5.036	0.223 - 113.569
No	2	61						
Pancreatic cannulation/injection								
Yes	2	31	1.041	0.308	0.627	0.658	1.872	0.117 - 30.014
No	6	214						
Pre-cut								
Yes	1	72	1.076	0.300	-3.848	0.055	0.021	0.000 - 1.086
No	7	173						
Papillotomy								
Yes	7	224	0.151	0.698	-0.646	0.640	0.524	0.035 - 7.837
No	1	21						

* Calculation is unfeasible because one of the comparable groups contains 0 cases.

In variety of prospective and retrospective studies, there were some differences in risk factors for PEP, which may be connected with definitions, technique, patients' inclusion criteria and especially the indication for ERCP. It is well known that in case of sphincter of Oddi dysfunction PEP incidence is significantly higher [3, 10, 12]. Besides, the sphincter of Oddi dysfunction, an example may be malignant biliary obstruction when some special factors, such as level of obstruction [19] and pancreatic duct obstruction, [2, 19] may play a role in PEP incidence.

That is why we have been focused on PEP in a particular group of patients – with choledocholithiasis. It seemed to us reasonable to investigate the homogeneous group of patients with a certain most common pathology for ERCP – choledocholithiasis to clarify PEP risk factors without impact connected with other diseases.

To obtain pure results we have analysed only the cases with naïve papilla and excluded patients with Billroth II gastrectomy, which have some features of endoscope intubation and biliary canulation. We also have not included patients with complications, such as biliary

pancreatitis and/or cholangitis and with an ampulla impacted stone.

We have carefully chosen the variables to be studied and intentionally have not taken such factors as smoking, drinking and comorbidities, which appear in other studies [4, 9]. We consider them irrelevant to PEP, though, this decision might be quite subjective. Unfortunately, we have not had data about history of pancreatitis, so we have not been able to take into account this important factor like in other works [4, 9-12], though results on this factor are controversial. We also have not considered the factor of difficult canulation as in our technique manner pre-cut papillotomy was done in case of it.

We have taken all the variables into multivariate regression as there is an opinion that such a model may give more reliable results [5, 20].

In our study the incidence of PEP is in line with those reported in other series, but comparison may be difficult, because we have investigated only the cases of choledocholithiasis and other works mainly represent variety of different conditions when ERCP was used [13-17]. In spite of not very huge number of patients and quite a few cases with PEP, we have managed to obtain statistically reliable data. The limitation in PEP cases did not allow us to make a multivariate analysis for blood bilirubin level, type of choledocholithiasis and ERCP success. However, by Chi-square test these factors turned out to be insignificant.

Some works show that young age [3, 11, 14, 17] or female gender [15, 16] or both of them [2, 5] may be independent factors for PEP. Our data show no influence of gender and age on PEP incidence. Such results were obtained in other studies as well [4, 9, 13].

No significant connection (P>0,05) has been found also for such factors as periampullary diverticulum, selective biliary cannulation, pancreatic cannulation/injection, pre-cut of papillotomy. Some of these factors turned out to be risk factors for PEP according several studies [3, 4, 5, 11, 12, 14].

By univariate analysis among all factors two have had significant connection with PEP – common bile duct ≤10 mm and papilla ≤5 mm (P=0.045, P=0.036 respectively).

But the only one appeared an independent risk factor – common bile duct ≤10 mm (P=0.018). This factor corresponds to other studies [13, 16]. But in these works, borderline value of CDB were 9 and 12 mm respectively.

The reason why common bile duct size has influence on PEP is not clear. We may suppose that higher biliary pressure in case of larger common bile duct (>10 mm) prevents PEP. On the contrary, subnormal pressure with common bile duct ≤10 mm is associated with increased incidence of PEP. The pathophysiology of that effect is to be investigated in the future.

Apart from the common bile duct size, according to the multivariate analysis there are factors with modulus of B-coefficient value ≥1,0 (table 2). That means that these factors (age, periampullary diverticulum, papilla size, selective biliary cannulation, Pre-cut) may have influence on the development of PEP. So further investigations with lager number of cases are needed to clear it up.

CONCLUSIONS

Our data shows that in patients with choledocholithiasis the occurrence of PEP is related to common bile duct size less than 10 mm. So small common bile duct was the only risk factor for PEP in patients with choledocholithiasis.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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