Risk Factors for post-Endoscopic Retrograde Cholangiopancreatography Abdominal Pain in Patients without post-ERCP Pancreatitis

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Abstract

Background: Most of the studies on the abdominal pain associated with endoscopic retrograde cholangiopancreatography (ERCP) are aimed at solving the pain during the procedure. Post-ERCP abdominal pain has rarely been investigated and few studies have focused on the characteristics and risk factors of post-ERCP abdominal pain without post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP). This study aimed to identify risk factors of post-ERCP abdominal pain without PEP and investigate characteristics of the abdominal pain in non-PEP patients.

Methods: From August 6th, 2019, to January 15th, 2020, data of patients who underwent ERCP were retrospectively collected. The characteristics of the abdominal pain after ERCP were recorded and compared between PEP and non-PEP patients. Multivariate analysis was conducted to identify risk factors of non-PEP abdominal pain.

Results: Data from 616 ERCP procedures were retrospectively investigated in this study, among which 51 (8.28%) patients presented post-ERCP abdominal pain without PEP and 45 (7.31%) patients developed PEP. Multivariate analysis found that 5 risk factors were associated with non-PEP abdominal pain: female gender (OR:2.137), upper abdominal surgery history (OR:1.948), first time ERCP (OR:4.735), elevated serum γ -glutamyl transferase (γ -GT) (OR:2.570) and elevated serum direct bilirubin (DBIL) (OR:2.932). Visual analogue scale (VAS) score of PEP abdominal pain was higher than that of non-PEP pain group ($P=0.05$). There were no significant differences in the time of the onset of the pain, pain relief time, pain frequency, use of analgesic medicine, hospital stay and mortality between PEP and non-PEP pain group ($P<0.05$).

Conclusion: This study indicated that female gender, upper abdominal surgery history, first time ERCP, elevated γ -GT and elevated DBIL were independent risk factors for post-ERCP abdominal pain without PEP. Abdominal pain was severer in PEP patients than non-PEP patients.

Introduction

Abdominal pain is often observed in patients after endoscopic retrograde cholangiopancreatography (ERCP) procedure, which sometimes indicates the occurrence of complications such as post-ERCP pancreatitis, perforation, or cholangitis. The most common complication with post procedure abdominal pain is acute pancreatitis, which occurs in 3.5%-14.7% of the cases^[1, 2] and leads to death in 0.1–1.1% of the patients^[2, 3]. For clinicians, fear of severe complication with abdominal pain may lead to anxiety and excessive treatment. Moreover, post-ERCP pain may influence the satisfaction and mental state of patients.

Most of the researches on the abdominal pain associated with ERCP are aimed at solving the pain during the procedure^[4]. Post-ERCP abdominal pain is one of the major symptoms of PEP; however, abdominal pain after the procedure also indicates potential occurrence of post-ERCP cholangitis, perforation and

nonspecific etiology (flatulence, gastric and intestinal spasm, etc.). Few studies have focused on the characteristics and risk factors of post-ERCP abdominal pain without PEP.

Therefore, this study aimed to identify the characteristics and risk factors of post-ERCP abdominal pain without PEP. Differences between abdominal pain with or without PEP were compared so as to guide clinical diagnosis and decision-making.

Methods

Study design and patients

In this retrospective study, all patients who underwent ERCP from August 6th, 2019, to January 15th, 2020, at Nanjing Medical University Affiliated Drum Tower Clinical Medical College were included. Exclusion criteria included any of the following: 1) failed operation; 2) missing any of the indicators. The Medical Ethics Committee of Nanjing Medical University Affiliated Drum Tower Clinical Medical College approved this retrospective data only study with waiver of informed consent. The need for individual consent was waived for retrospective cohorts.

Data collection

The following data were extracted from the medical charts: patient-related (sex, age, surgical history, gastrectomy history, cholecystectomy history, drinking history, smoking history, hypertension, diabetes, coronary heart disease, chronic pancreatitis history, acute pancreatitis history, white blood cells(WBC), hemoglobin(Hb), platelet(PLT), neutrophil percentage(Neut%), alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ -glutamyl transferase (γ -GT), total bilirubin(TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), albumin (ALB), prothrombin time (PT), history of pancreatic diseases, suspicion of sphincter of Oddi dysfunction (SOD), hilar bile duct stricture, distal biliary stricture, diagnosis of common bile duct stone, and adenoma of the duodenal papilla); procedure-related (pre-cut, endoscopic sphincterotomy, pancreatic guidewire passages, biliary stent placement, endoscopic papillary balloon dilatation(EPBD), endoscopic papillary large-balloon dilation(EPLBD), nasobiliary drainage, difficult biliary cannulation (cannulation attempts of duration > 10 minutes, and/or > 5 attempts), contrast injection to the pancreatic duct, dilated extrahepatic bile duct, type of papillary orifice, pancreatic duct stenting and operator experience (high grade: >200 ERCP procedures total and/or > 50/year); postoperative outcomes(Visual analogue scale(VAS) score of post-ERCP abdominal pain, time of the onset of post-ERCP pain, pain relief time, pain frequency, use of analgesic medicine, use of protease inhibitors, total hospital stay, hospital stay after ERCP. Indomethacin suppository was given routinely as per the judgment of the operator. If the patient had new or aggravated epigastric pain within 72 hours after procedure, abdominal imaging was routinely performed according to the general situation of the patient, and, if necessary, protease inhibitors or analgesic medicine was given.

Definitions

PEP is diagnosed with 2 out of 3 diagnostic criteria defined by the Revised Atlanta Classification (pancreatic abdominal pain, three times upper limit of normal elevation of serum lipase, imaging suggestive of pancreatitis). Post-ERCP cholangitis is defined as new onset of fever ($> 38^{\circ}\text{C}$, lasting over 24 hours) and cholestasis. Post-ERCP perforation is defined with imaging evidence of gas or luminal contents outside of the gastrointestinal tract. Post-ERCP bleeding is diagnosed with hematemesis and/or melena or hemoglobin drop $> 2 \text{ g/dL}$ or bloody fluid from nasobiliary drainage. Severity grading is conformed with ESGE guideline 2019^[5]. Post-ERCP abdominal pain is diagnosed as a new or aggravated upper abdominal pain within 72 hours after ERCP.

Statistical analysis

The continuous data were dichotomized according to the cut-off value of each indicator based on clinical significance or normal range. Categorical data were expressed as numbers, rates, and percentages and were compared with the chi-square test or Fisher's test. The relevant factors found by univariate analyses ($P < 0.15$) were included in the multivariate logistic regression analysis (forward stepwise regression selection). A receiver operating characteristics (ROC) curve was used to examine the sensitivity and specificity, and the area under the ROC curve (AUC) was used for discrimination.

Propensity score matching was performed to compare the realistic difference between PEP group and non-PEP group with post-ERCP abdominal pain. Prior to propensity matching, t tests or Chi-Square tests were used to assess for differences between groups. PEP group and non-PEP pain group were matched 1:1 on the following variables: age, gender, comorbidities (coronary heart disease, diabetes, hypertension, chronic liver disease, malignant tumors or cancer, chronic pancreatitis), surgery history, operation time, laboratory tests before operation (complete blood count, liver function test, kidney function test, prothrombin time (PT), CA199). McNemar's test was used for binary variables. And a paired Student's t-test or paired-sample test was used for continuous variables. Statistical significance was treated as a p-value < 0.05 . All data were analyzed using SPSS 25.

Results

Characteristics of the patients

Data of 616 patients who underwent ERCP from August 6, 2019, to January 15, 2020 were retrospectively collected. Among these patients, 45 developed post-ERCP pancreatitis, and 51 presented post-ERCP abdominal pain without PEP, including 11 post-ERCP cholangitis, 1 mild bleeding and 39 nonspecific abdominal pain. The rest 520 patients did not have any abdominal pain after operation. Patients' characteristics between normal group and non-PEP pain group were presented in Table 1.

Univariate analysis

In the univariate analysis, 14 of 46 patient-related factors and 9 of 23 procedure-related factors were found to be associated with an increased risk of post-ERCP abdominal pain without PEP (Table 1).

Patient-related risk factors included: female gender, age <60 yr, no hypertension, first time ERCP, no drinking history, normal neut%, lower Hb, normal ALT, elevated γ -GT, normal TBIL, elevated DBIL, normal ALP, normal ALB, normal CA199. Procedure-related risk factors included: rectal indomethacin, native papilla, difficult cannulation, pancreatic guidewire passages, contrast injection to the pancreatic duct, absence of EPLBD, absence of brush cytology, absence of biliary stent placement, pancreatic duct stenting.

Multivariate analysis

Risk factors that reached a p-value cut-off 0.15 or less were used to create the multivariate model. Variables which were considered to be the risk factors according to clinical experience and previous researches were also analyzed. The identified factors were entered into multivariate model (Table 2). Five risk factors were significant by multivariate analysis, three were characteristics of the patients (female gender, first time ERCP, upper abdominal surgery history), and two were preoperative laboratory examinations (elevated serum γ -GT and DBIL before ERCP) (Figure 2). The Hosmer-Lemeshow goodness of fit test was not significant($p=0.982$) at the 0.05 significance level and the C-statistic was 0.764.

Table 2. Multivariate analyses (C-statistic = 0.764)

Risk Factors	β	Odds Ratio	95% Confidence Interval	<i>p</i> value
Gender(female)	0.759	2.137	1.152-3.962	0.016
Primary ERCP	1.555	4.735	1.886-11.889	0.001
γ -GT	0.944	2.570	1.299-5.085	0.007
DBIL	1.076	2.932	1.356-6.341	0.006
Upper abdominal surgery history	0.667	1.948	1.009-3.761	0.047

γ -GT: γ -glutamyl transferase; DBIL: direct bilirubin.

Propensity matching between PEP group and non-PEP pain group

In order to identify the characteristics of the post-ERCP pain without PEP, PEP group and non-PEP pain group were compared and analysed. Before propensity matching, there were differences between the PEP group and non-PEP pain group in baseline characteristics. With the use of propensity matching, 34 patients with PEP were matched with 34 patients with non-PEP abdominal pain. The baseline characteristics were comparable after propensity matching (Table 3). Characteristics between two groups were similar in the time of the onset of the pain, pain relief time and pain frequency($P<0.05$) (Table.4). It showed that pain intensity—expressed as VAS score—of post-ERCP abdominal pain related to PEP was higher than that of non-PEP pain. ($P=0.05$). There were no significant differences in the use of analgesic medicine, hospital stay and mortality between the two groups.

Table 4. Characteristics between non-PEP group and PEP group

	Non-PEP group n=34(%)	PEP group n=34(%)	<i>p</i> value
Total hospital stay (days)	10.15±8.894	13.71±17.85	0.214
Hospital stay after ERCP (days)	7.38±8.59	10.56±13.22	0.244
Mortality	1	0	1.000
Time of the onset of pain(hours)	13.19±16.44	9.04±7.76	0.193
VAS score	3.68±1.81	4.50±1.36	0.050
Pain relief time(hours)	1.98±3.59	1.39±2.07	0.412
Pain frequency(times)	1.41±1.28	1.60±1.20	0.524
Analgesic medicine use	22	27	0.280
Protease inhibitors use	13	31	0.000

Discussion

Abdominal pain after ERCP is common and is a source of distress to both patient and physician. Occasionally it predicts complications related to the procedure, especially PEP. However, apart from PEP, some postprocedural pain is of other etiology: 1. Post-ERCP cholangitis, typically presenting with fever, jaundice, and abdominal pain, needing use of anti-biotics or repeated ERCP; 2. Perforation, manifested as severe abdominal and back pain, abdominal tenderness and fever, needing intensive management, even surgery; 3. Nonspecific pain, often resolving in several hours. Several reports considered nonspecific pain may in part relate to bowel insufflation with air^[4, 6]. According to typical clinical symptoms, it is relatively easier to identify perforation, bleeding and cholangitis. Therefore, it is a challenge for early differentiating between the pain of PEP and nonspecific pain. Empirical data on post-ERCP abdominal pain can be used to optimize the information for patients undergoing ERCP. It may contribute to improvement of a patient's tolerance and the practice guidelines of support treatment, because such data enable better preparation of both patients and physician for the procedure.

In our study, 51 non-PEP pain patients consist of 11 mild post-ERCP cholangitis, 1 mild bleeding and 39 nonspecific pain. Our results showed that non-PEP pain was associated with female gender, first time ERCP and upper-abdominal surgery history, as well as patient's elevated pre-ERCP serum γ -GT and DBIL level. Female gender was found to be the risk factor for post-ERCP abdominal pain without PEP in this study. Tom B. Glomsaker^[7] found that female patients demonstrated an increased risk for reporting pain both during and after the ERCP procedure. Though this study did not exclude patients with PEP, this finding is partly in agreement with our result. Patients who underwent ERCP for the first time have a

higher risk of abdominal pain after ERCP. Essink-Bot et al.^[8] found that patients who had undergone previous surveillance endoscopies for Barrett's esophagus experienced less discomfort, pain, and overall burden than patients who underwent upper endoscopy for the first time. They suggested that these previous surveillance endoscopies had resulted in an adaptation to the procedure. Upper-abdominal surgery history may cause postoperative abdominal adhesions and alter anatomy which would increase operative difficulty and probability of postoperative abdominal pain. Karayiannakis et al.^[9] reported that adhesions in patients with upper-abdominal surgery occurred more frequently, and were more extensive and denser than those in patients with lower-abdominal surgery. It explains why no significant difference in the history of lower-abdominal surgery or the history of all types of surgery between groups was found in our study. Moreover, our study found that elevated serum γ -GT and DBIL before the procedure were risk factors for post-ERCP pain. In contrast, elevated serum DBIL was proved to be protective factors for PEP^[10], which means that if patients with abnormal DBIL present abdominal pain after ERCP, it is more likely to be other etiology rather than PEP.

Most clinicians would agree that patient satisfaction is of great importance. Patient satisfaction related to the ERCP procedure is related to the patients' experiences of pain during and after the procedure regularly^[7]. Nonspecific pain after ERCP may be confused with early symptom of complications, which influences clinical treatment and causes patients' postoperative anxiety. After propensity-score matching, we found that the pain intensity related to PEP was more severe than that without PEP (4.50 ± 1.36 vs. 3.68 ± 1.81 , $p = 0.050$). Our result was consistent with that of the previous studies. JSGE guideline for post-ERCP pancreatitis^[11] showed that strong abdominal pain indicates a high probability of PEP. Hauser G et al.^[12] found a threshold VAS score of 5 was strongly associated with the occurrence of PEP. They suggested that the VAS scores for abdominal pain appear to have an excellent diagnostic value for predicting both the presence and absence of PEP. Thus, VAS score may help distinguishing these two types of pain. For this study, it was reasonable to find protease inhibitors were used more frequently in PEP cases. The use of analgesic medicine was similar between PEP group and non-PEP pain group. Clinicians tended to give analgesic medicine rather than protease inhibitors to relief pain firstly in our study. It indicated that non-PEP pain especially nonspecific pain may lead to analgesic abuse.

Our study has limitations. This is a retrospective, observational study and hence suffers from potential selection and ascertainment bias despite propensity-score matching. Larger sample sizes or prospective studies are necessary to reduce biases.

Conclusion

In conclusion, our study indicated that female gender, first time ERCP, elevated serum γ -GT, elevated serum DBIL and upper abdominal surgery history were independent risk factors for post-ERCP abdominal pain without PEP. Characteristics of post-ERCP pain were different in VAS score between PEP patients and non-PEP pain patients. These findings may contribute to the relief of patients' discomfort and dissatisfaction and therefore improve the quality of ERCP procedures and patient management.

Abbreviations

ERCP

Endoscopic retrograde cholangiopancreatography; PEP:Post-ERCP pancreatitis; VAS:Visual analogue scale; OR:Odds ratio; EPBD:Endoscopic papillary balloon dilatation; EPLBD:Endoscopic papillary large-balloon dilation(EPLBD); AUC:Area under the curve; ROC:Receiver operating characteristic curve

Declarations

Ethics approval and consent to participate

The study was approved by the Ethical Committee at Nanjing Drum Tower Hospital Affiliated to Nanjing University Medical School. The Ethical Committee at Nanjing Drum Tower Hospital Affiliated to Nanjing University Medical School approved the waiver of consent.

Consent for publication

Not applicable.

Availability of data and materials

The data set analyzed in the current study cannot be opened to public because patients' privacy must be protected and IRB does not permit to do so. However, data are available from the author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XZ and LW designed the research and the study concept; MC and RZ contributed to analysis and interpretation of data; JC and YY contributed to the acquisition of data. MC and RZ wrote the paper. XZ and LW supervised the study; all of the co-authors conducted a critical revision of the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

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Tables

Table 1. Univariate analyses

	Normal groupn%	Non-PEP pain groupn%	p
Gender(female)	213/52040.96	35/5168.63	0.003
Age(<60yr)	193/52037.12	28/5154.90	0.016
Past history	358/52068.85	32/5162.75	0.430
Hypertension	196/52037.69	12/5123.53	0.048
Coronary heart disease	34/5206.54	2/513.92	0.666
Diabetes	94/52018.08	9/5117.65	1.000
Hepatitis	43/5208.27	6/5111.76	0.556
Tuberculosis	6/5201.15	2/513.92	0.155
Malignancy	15/5202.88	1/511.96	1.000
Acute pancreatitis	16/5203.08	1/511.96	0.987
Chronic pancreatitis	18/5203.46	2/513.92	1.000
Cirrhosis	24/5204.62	0/510	0.229
Fatty liver	28/5205.38	0/510	0.174
Allergy history	41/5207.88	6/5111.76	0.487
Transfusion history	22/5204.23	1/511.96	0.679
Surgical history	452/52086.92	43/5184.31	0.665
First time ERCP	381/52073.27	44/5186.27	0.044
Upper abdominal surgery history	264/52050.77	30/5158.82	0.306
Lower abdominal surgery history	104/52020.00	8/5115.69	0.474
Orthopedic surgery	22/5204.23	1/511.96	0.679
Cardiothoracic surgery	32/5206.15	2/513.92	0.739
Head and neck surgery	22/5204.23	1/511.96	0.679
Gastrectomy history	14/5202.69	2/513.92	0.530
Trauma history	25/5204.81	3/515.88	1.000
Smoking history	96/52018.46	8/5115.69	0.708
Drinking history	69/52013.27	2/513.92	0.071
WBC≤9.5	442/52085.00	46/5190.20	0.407
N rate≤75%	375/52072.12	42/5182.35	0.068
Hb≤120	307/52059.04	37/5172.55	0.072
PLT (≥125	416/52080.00	44/5186.27	0.355
ALT (≤40)	217/52041.73	31/5160.78	0.011
AST (≤40)	272/52052.31	30/5158.82	0.383
γ-GT (>35)	433/52083.27	30/5158.82	0.000
BIL (≤28)	281/52054.04	39/5176.47	0.003
DBIL (>10)	261/52050.19	10/5119.61	0.000
ALP (≤185)	313/52060.19	40/5178.43	0.015
ALB (≥40)	128/52024.62	19/5137.25	0.064
PT (≤15)	482/52092.69	50/5198.04	0.249
AMY (≤110)	360/52069.23	34/5166.67	0.751
CA199 (≤27)	326/52062.69	40/5178.43	0.031
Pancreatic diseases	44/5208.46	7/5113.73	0.317
Common bile duct stone	338/52065.00	32/5162.75	0.760
Hilar bile duct stricture	66/52012.69	3/515.88	0.182
Distal biliary stricture	94/52018.08	8/5115.69	0.710

SOD	2/5200.38	1/511.96	0.245
Duodenal papilla carcinoma	12/5202.31	3/515.88	0.287
Operator experience (high grade)	231/52044.42	23/5145.10	1.000
Operative time(<60min)	472/52090.77	50/5198.04	0.132
Indomethacin	8/5201.54	4/517.84	0.013
Native orifice	350/52067.31	40/5178.43	0.116
Peri-diverticular papilla	108/52020.77	8/5115.69	0.468
Intra-diverticular papilla	15/5202.88	2/513.92	1.000
Difficult biliary cannulation	51/5209.81	9/5117.65	0.093
Pancreatic guidewire passages	176/52033.85	25/5149.02	0.033
Contrast injection to the pancreatic duct	83/52015.96	13/5125.49	0.114
Dilated extrahepatic bile duct	403/52077.50	39/5176.47	1.000
Papilla opening	338/52065.00	33/5164.71	1.000
EST	281/52054.04	31/5160.78	0.380
EPBD	58/52011.15	4/517.84	0.502
EPLBD	103/52019.81	5/519.80	0.092
Pre-cut	21/5204.04	4/517.84	0.364
Titanium clip	30/5205.77	2/513.92	0.819
Stone extraction	326/52062.69	32/5162.75	1.000
Nasobiliary drainage	339/52065.19	38/5174.51	0.216
Bile duct brush	57/52010.96	2/513.92	0.148
IDUS	26/5205.00	0/5100	0.200
Spyglass	11/5202.12	0/5100	0.611
Biliary stent placement	118/52022.69	5/519.80	0.048
Pancreatic duct stenting	129/52024.81	19/5137.25	0.065
Hyperamylasemia	283/52054.42	28/5154.90	1.000
Postoperative WBC $\leq$ 9.5	71/52013.65	8/5115.69	0.832
Postoperative N rate $\leq$ 75%	223/52042.88	24/5147.06	0.657
Postoperative fever	122/52023.46	13/5125.49	0.863
Antibiotic after procedure	220/52042.31	17/5133.33	0.236
Postoperative septic shock	7/5201.35	1/511.96	0.529
Postoperative hemorrhage	10/5201.92	1/511.96	1.000
Post-ERCP cholangitis	114/52021.92	11/5121.57	1.000
Nonspecific abdominal pain	/	39/5176.47	/
Operation for adverse effects	1/5200.19	0/5100	1.000
Protease inhibitors after procedure	165/52031.73	21/5141.18	0.210

PEP: post-ERCP pancreatitis; WBC: white blood cells; Hb: hemoglobin; PLT: platelet; ALT: alanine aminotransferase; AST: aspartate aminotransferase; γ -GT: γ -glutamyl transferase; BIL: total bilirubin; DBIL: direct bilirubin; ALP: alkaline phosphatase; ALB: albumin; PT: prothrombin time; AMY: serum amylase; SOD: superoxide dismutase; EST: endoscopic sphincterotomy; EPBD: endoscopic papillary balloon dilation; EPLBD: endoscopic papillary large-balloon dilation

Table 3. Baseline characteristics and procedure characteristics before and after Propensity matching

Variables	Before matching			After matching		
	Pain without PEP	Pain with PEP	P value	Pain without PEP	Pain with PEP	P value
	n=510%	n=450%		n=340%	n=340%	
Gender(female)	32062.75	18040.00	0.040	18052.94	15044.12	0.628
Age(<60yr)	23045.10	24053.33	0.540	20058.82	17050.00	0.627
Past history	32062.75	28062.22	0.562	21061.76	23067.65	0.800
Hypertension	12023.53	10022.22	1.000	6017.65	9026.47	0.560
Coronary heart disease	203.92	102.22	1.000	102.94	102.94	1.000
Diabetes	9017.65	408.89	0.246	6017.65	4011.76	0.734
Hepatitis	6011.76	306.67	0.495	4011.76	205.88	0.673
Tuberculosis	203.92	000	0.497	000	000	/
Malignancy	101.96	102.22	1.000	102.94	102.94	1.000
Acute pancreatitis	101.96	102.22	1.000	102.94	102.94	1.000
Chronic pancreatitis	203.92	204.44	1.000	205.88	102.94	1.000
Cirrhosis	000	102.22	0.469	000	000	/
Fatty liver	000	204.44	0.217	000	000	/
Allergy history	6011.76	6013.33	1.000	6017.65	6017.65	1.000
Transfusion history	101.96	204.44	0.598	102.94	205.88	1.000
Surgical history	43084.31	42093.33	0.209	29085.29	32094.12	0.427
Primary ERCP	44086.27	37082.22	0.779	27079.41	27079.41	1.000
Upper abdominal surgery history	30058.82	19042.22	0.152	24070.59	16047.06	0.084
Lower abdominal surgery history	8015.69	7015.56	1.000	4011.76	4011.76	1.000
Orthopedic surgery	101.96	204.44	0.598	000	205.88	0.493
Cardiothoracic surgery	203.92	102.22	1.000	102.94	102.94	1.000
Head and neck surgery	101.96	000	1.000	000	000	/
Gastrectomy history	305.88	204.44	1.000	205.88	205.88	1.000
Trauma history	305.88	306.67	1.000	205.88	308.82	1.000
Smoking history	8015.69	10022.22	0.444	7020.59	9026.47	0.776
Drinking history	203.92	5011.11	0.247	102.94	308.82	0.614
WBC≤9.5	509.80	5011.11	1.000	5014.71	4011.76	1.000
N rate≤75%	8015.69	5011.11	0.564	6017.65	4011.76	0.734
Hb≤120	14027.45	8017.78	0.333	11032.35	6017.65	0.262
PLT (≥125	7013.73	5011.11	0.765	102.94	4011.76	0.356
ALT (≤40)	20039.22	26057.78	0.101	11032.35	17050.00	0.218
AST (≤40)	21041.18	21046.67	0.681	12035.29	12035.29	1.000
γ-GT (>35)	21041.18	13028.89	0.285	15044.12	13038.24	0.806
BIL (≤28)	12023.53	15033.33	0.364	8023.53	7020.59	1.000
DBIL (>10)	41080.39	30066.67	0.163	27079.41	27079.41	1.000
ALP (≤185)	11021.57	15033.33	0.251	8023.53	8023.53	1.000
ALB (≥40)	32062.75	23051.11	0.535	22064.71	18052.94	0.460
PT (≤15)	50098.04	43095.56	0.598	33097.06	33097.06	1.000
CA199 (≤27)	11021.57	15033.33	0.251	7020.59	11032.35	0.410
Pancreatic diseases	7013.73	6013.33	1.000	6017.65	6017.65	1.000
Common bile duct stone	32062.75	26057.78	0.679	19055.88	19055.88	1.000
Hilar bile duct stricture	305.88	408.89	0.702	205.88	205.88	1.000
Distal biliary stricture	8015.69	8017.78	1.000	7020.59	6017.65	1.000

SOD	111.96	000	1.000	112.94	000	1.000
Duodenal papilla carcinoma	315.88	316.67	1.000	112.94	318.82	0.614
Operator experience (high grade)	23145.10	22148.89	0.838	17150.00	18152.94	1.000
Operative time	33.69±16.53	44.69±25.10	0.015	37.00±17.54	42.24±18.22	0.232
Cannulation time	2.89±3.61	6.86±11.77	0.034	3.26±3.95	5.29±8.29	0.204
Native orifice	40178.43	39186.67	0.422	25173.53	29185.29	0.369
Peri-diverticular papilla	8115.69	16135.56	0.034	6117.65	11132.35	0.262
Intra-diverticular papilla	213.92	112.22	1.000	112.94	112.94	1.000
Cannulation frequency	2.71±2.17	3.96±5.257	0.123	2.76±2.24	4.03±5.82	0.241
Difficult biliary cannulation	9117.65	12126.67	0.329	7120.59	8123.53	1.000
Pancreatic guidewire passages	25149.02	26157.78	0.419	20158.82	21161.76	1.000
Contrast injection to the pancreatic duct	13125.49	13128.89	0.819	11132.35	12135.29	1.000
Frequency of pancreatic guidewire passages	0.78±0.94	1.16±1.61	0.165	0.88±0.88	0.97±1.03	0.705
Dilated extrahepatic bile duct	39176.47	28162.22	0.181	24170.59	18152.94	0.212
Papilla opening	33164.71	316.67	0.387	20158.82	23167.65	0.615
EST	31160.78	30166.67	0.671	19155.88	20158.82	1.000
EPBD	417.84	6113.33	0.586	215.88	6117.65	0.259
EPLBD	519.80	8117.78	0.371	5114.71	7120.59	0.752
Pre-cut	417.84	418.89	1.000	4111.76	215.88	0.673
Titanium clip	213.92	316.67	0.663	112.94	318.82	0.614
Stone extraction	32162.75	27160.00	0.835	19155.88	20158.82	1.000
Nasobiliary drainage	38174.51	27160.00	0.189	26176.47	20158.82	0.164
Bile duct brush	213.92	5111.11	0.247	000	318.82	0.239
IDUS	000	214.44	0.217	000	112.94	1.000
Spyglass	000	112.22	0.469	000	112.94	1.000
Biliary stent placement	519.80	5111.11	1.000	4111.76	318.82	1.000
Pancreatic duct stenting	19137.25	18140.00	0.835	15144.12	15144.12	1.000
Hyperamylasemia	28154.90	44197.78	0.000	19155.88	33197.06	0.000
Postoperative WBC1≤9.5	8115.69	17137.78	0.019	8123.53	11132.35	0.590
Postoperative N rate1≤75%	24147.06	36180.00	0.001	21161.76	26176.47	0.294
Postoperative fever	13125.49	23151.11	0.012	11132.35	14141.18	0.615
Antibiotic after procedure	17133.33	25155.56	0.023	12135.29	17150.00	0.327
Postoperative septic shock	111.96	316.67	0.338	000	215.88	0.439
Postoperative hemorrhage	111.96	000	1.000	000	000	/
Post-ERCP cholangitis	11121.57	19141.30	0.046	9126.47	10129.41	1.000
nonspecific abdominal pain	39176.47	/	/	25173.52	/	/
Operation for adverse effects	000	000	/	000	000	/

Figures

Figure 1

ROC curve for risk of post-ERCP pain without PEP

Figure 2

Forrest plot for the factors involved in the risk of post-ERCP pain without PEP