



# The Risk Factors of Early Biliary Infection After <sup>125</sup>I Particles Stent Implantation in Patients with Malignant Biliary Obstruction

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## Abstract

**Background:** Early biliary infection (EBI) is a significant and prevalent complication following percutaneous transhepatic biliary stenting, especially in cases involving the use of <sup>125</sup>I particle stents for malignant biliary obstruction (MBO).

**Objectives:** This study aims to uncover potential risk factors contributing to EBI post-implantation in this patient group.

**Patients and Methods:** In this retrospective study, a total of 231 patients who underwent <sup>125</sup>I particle stent implantation between January 2014 and December 2020 were included. Screening based on inclusion/exclusion criteria identified a total of 178 patients (115 males and 63 females, aged 32 - 83 years). Early biliary infection occurrence was monitored within the first 30 days following the stent implantation, when infectious complications are most prevalent. We analyzed baseline characteristics and perioperative parameters of patients, comparing those who developed EBI with those who did not. Multivariate logistic regression was employed to identify significant risk factors for EBI.

**Results:** Out of the 178 patients, 35 (19.7%) developed EBI within 30 days post-implantation. Every EBI case was accompanied by a positive bile culture. Notably, patients with EBI more frequently had diabetes [odds ratio (OR), 3.329; 95% confidence interval (CI), 1.129 - 9.819; regression coefficient (B) = 1.203; P = 0.029], gallstones in the gallbladder or bile ducts (OR, 3.459; 95% CI, 1.060 - 11.283; B = 1.241; P = 0.040), higher level of biliary obstruction (OR, 3.008; 95% CI, 1.243 - 7.280; B = 1.101; P = 0.015), intraoperative biliary bleeding (OR, 5.416; 95% CI, 1.569 - 18.696; B = 1.689; P = 0.008), and postoperative intrahepatic pneumobilia (OR, 2.655; 95% CI, 1.108 - 6.362; B = 0.976; P = 0.029) compared to those without EBI. These factors were positively correlated with EBI development post-implantation. Conversely, the duration from percutaneous transhepatic biliary drainage (PTBD) to <sup>125</sup>I stent implantation was longer in patients without EBI (OR, 0.966; 95% CI, 0.940 - 0.992; B = -0.035; P = 0.012), suggesting a negative association with EBI occurrence.

**Conclusion:** This study identifies diabetes, gallstones in the gallbladder or bile ducts, high-level obstruction, intraoperative biliary bleeding, and postoperative intrahepatic pneumobilia as significant risk factors for EBI. Additionally, a longer interval from PTBD to <sup>125</sup>I stent implantation emerges as a protective factor against EBI in patients with MBO undergoing <sup>125</sup>I particle stent implantation. These risk factors can offer guidance to minimize post-<sup>125</sup>I particle stent implantation biliary infection, thereby shortening hospitalization for affected patients.

**Keywords:** Early Biliary Infection, Percutaneous Transhepatic Biliary Drainage, Malignant Biliary Obstruction, <sup>125</sup>I Particles Stent Implantation, Risk Factor

## 1. Background

Malignant biliary obstruction (MBO) is a pathological blockage caused by malignancies in the bile duct, gallbladder, pancreas, ampulla of Vater, liver, etc. (1). Cholestasis in the bile duct can lead to the penetration of bile into the bloodstream. To avoid the adverse effects of hyperbilirubinemia, biliary drainage is necessary (2). A meta-analysis based on 26 articles revealed that preoperative biliary drainage improves the outcomes of malignant obstructive jaundice after surgery (3). For

patients unable to undergo surgery, percutaneous transhepatic biliary drainage (PTBD) and endoscopic biliary drainage are commonly used strategies (4).

Percutaneous transhepatic biliary stenting (PTBS) is a supplement to PTBD, which can dredge the biliary tract, normalize plasma levels of bilirubin, and relieve MBO-associated symptoms (5). In PTBS, metal stents are superior to plastic stents due to longer patency and lower re-intervention rates (6). However, the growth of tumor cells and mucosal hyperplasia significantly limit the cumulative patency rate of metal stents, leading to

the recurrence of biliary restenosis or obstruction (7). Encouragingly, the development of  $^{125}\text{I}$  particle stents opens new horizons. The implantation of  $^{125}\text{I}$  particle stents can not only dredge obstruction but also inhibit the growth of tumor cells in the bile duct (8). Pang et al. found that PTBS combined with  $^{125}\text{I}$  particles is more effective in inhibiting biliary re-obstruction and prolonging survival time than PTBS alone (9). Hasimu et al. also demonstrated that PTBS with  $^{125}\text{I}$  particles improves stent patency and extends survival time in patients with MBO (10). With the ability to prevent restenosis,  $^{125}\text{I}$  particle stent implantation shows great potential in the treatment of MBO.

With the widespread application of PTBS, increasing attention has been paid to complications. Early biliary infection (EBI) is a common early postoperative complication after PTBS, manifesting as shivering, fever, and even septic shock, posing a serious threat to patients' health and life (11). A previous study reported that  $^{125}\text{I}$  particle stent implantation is superior to conventional stents in reducing the risk of EBI, possibly due to the antimicrobial properties of integrated  $^{125}\text{I}$  and variations in stent composition, design, or material (12). Therefore, the prevention of EBI following  $^{125}\text{I}$  particle stent implantation is urgently needed.

Controlling risk factors is an effective strategy for preventing potential complications. Liu et al. revealed that diabetes, previous surgical or endoscopic treatment, procedure time > 60 min, and intraprocedural biliary hemorrhage are risk factors for EBI after PTBS (13). However, the risk factors of EBI following  $^{125}\text{I}$  particle stent implantation are not fully revealed. In this study, a total of 178 patients with MBO who underwent  $^{125}\text{I}$  particle stent implantation were enrolled. The baseline characteristics and perioperative parameters of these patients with or without EBI were retrospectively analyzed.

## 2. Objectives

This study aims to reveal potential risk factors of EBI after  $^{125}\text{I}$  particle stent implantation, providing guidance for the clinical treatment of MBO.

## 3. Patients and Methods

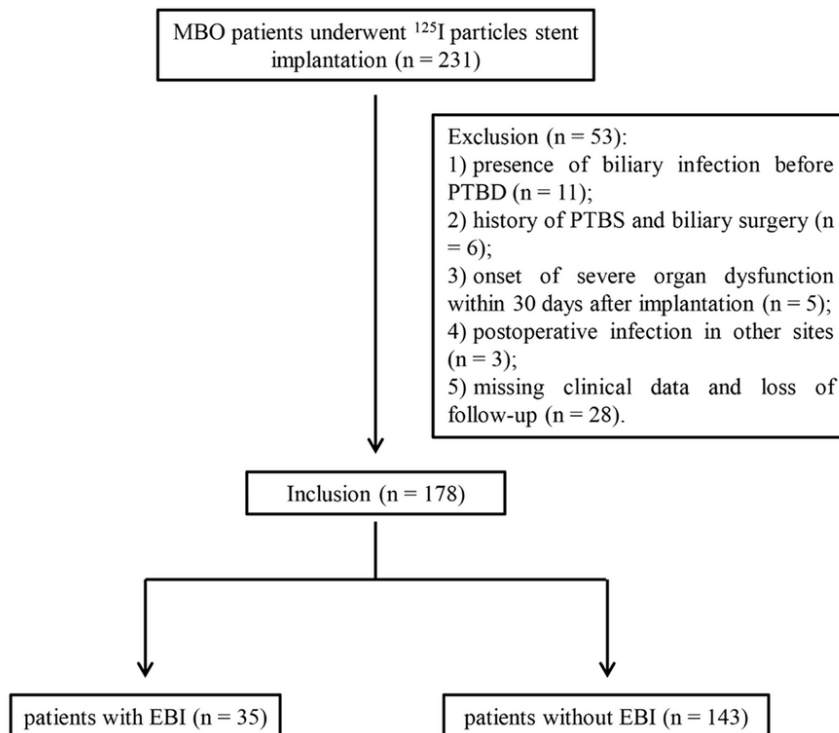
### 3.1. Subjects

This study received approval from the Ethics Committee of our hospital (ethical approval code: 2020-13). Informed consent was obtained from all cases.

As a retrospective study, a total of 231 patients who underwent  $^{125}\text{I}$  particle stent implantation were collected from our hospital between January 2014 and December 2020. All patients were diagnosed with MBO based on pathological and imaging examinations. The inclusion criteria included: (1) > 18 years old; (2) unable or unwilling to undergo surgical operation; (3) first-time stent implantation. The exclusion criteria included: (1) benign biliary obstruction; (2) presence of biliary infection before PTBD ( $n = 11$ ); (3) history of PTBS and biliary surgery ( $n = 6$ ); (4) onset of severe organ dysfunction within 30 days after implantation ( $n = 5$ ); (5) postoperative infection in other sites ( $n = 3$ ); (6) missing clinical data and follow-up information ( $n = 28$ ). Finally, a total of 178 patients (115 males and 63 females, aged 32 - 83 years) were included and analyzed in this study, comprising 35 patients with EBI and 143 patients without EBI (Figure 1). Patients included in the study underwent routine preoperative comprehensive assessments, including blood cell analysis, coagulation function tests, electrocardiography, liver and kidney function assessments, electrolyte analysis, abdominal computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography. The baseline data, including sex, age, liver function [total bilirubin (TBIL), direct bilirubin (DBIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and albumin (ALB)], blood routine [white blood cells (WBC), hemoglobin (HGB), and platelets (PLT)], coagulation function [prothrombin time (PT) and activated partial thromboplastin time (APTT)], comorbidity [diabetes mellitus (DM) and gallstones], obstruction location, and tumor types were collected.

### 3.2. $^{125}\text{I}$ Particles Stent Implantation

The biliary  $^{125}\text{I}$  particle stent was purchased from Nanjing Micro-Tech Co., Ltd. (Nanjing, China), with a diameter of 10 mm (Appendix 1). Before stent implantation, PTBD was performed to determine the location and length of the obstruction in the bile duct under the digital subtraction angiography suite (Appendix 2). A guide wire was introduced through the PTBD tube, and the outer sheath was replaced. Using a single-curved catheter alongside the guide wire, the catheter traversed the narrowed bile duct segment. After removing the guide wire, cholangiography through the catheter precisely located and determined the length of the obstructed segment (Appendix 2). A



**Figure 1.** Flow chart describing the study design (MBO, malignant biliary obstruction; PTBD, percutaneous transhepatic biliary drainage; EBI, early biliary infection).

260 cm super-stiff, extra-long guide wire was then exchanged before withdrawing the catheter (Appendix 2). The number of  $^{125}\text{I}$  particles (diameter = 0.8 mm, length = 4.5 mm, effective radiation radius = 17 mm, half-life = 59.43 days; Beike Biotechnology, Beijing, China) was calculated by the radiotherapy treatment planning system (HGGR-2000; Hokai Medical Instruments, Zhuhai, China) according to the tumor status. The  $^{125}\text{I}$  particles are disinfected using 75% alcohol or high-temperature/high-pressure methods. They are then secured onto the particle stent delivery device using forceps. While loading  $^{125}\text{I}$  particles, avoid withdrawing the central metal support rod of the delivery device assembly. The biliary  $^{125}\text{I}$  particle stent is guided to the lesion site along a super-stiff guidewire and released upon confirming precise positioning using the proximal method (Appendix 2). After withdrawing the  $^{125}\text{I}$  particle stent delivery system, a standard biliary stent is advanced along the super-stiff guidewire to the site of bile duct obstruction (Appendix 2). The regular biliary stent is positioned to overlap with the

radioactive particle stent, ensuring approximately a 10 mm extension beyond the lesion's upper and lower margins. Contrast imaging is then performed to confirm the release position and deployment status of the stent. Finally, the PTBD external drainage catheter (Cook Medical, USA) is to be retained in place and secured with appropriate dressing (Appendix 2).

Both PTBD and  $^{125}\text{I}$  particle stent implantation were performed by professional senior physicians. After the implantation for 2-3 weeks, unobstructed bile drainage was identified by cholangiography. Within 30 days after implantation, EBI was identified by the characteristics of fever ( $\geq 37.3^\circ\text{C}$ ), persistent increase in white blood cells and neutrophils, positive bile culture, pain around the liver region, and/or continuous progression of jaundice. EBI within the initial 30 days post-stent implantation is consistent with clinical norms, emphasizing the critical early period when infectious complications are most prevalent.

For patients who develop EBI after  $^{125}\text{I}$  particle stent placement, if the PTBD drainage tube is not removed, biliary drainage can be performed through the PTBD

**Table 1.** Baseline Characteristics of Patients with and Without Early Biliary Infection

Parameters	Non-EBI (n = 143)	EBI (n = 35)	P-value
<b>Sex</b>			0.809
Male	93 (65.0)	22 (62.9)	
Female	50 (35.0)	13 (37.1)	
<b>Age (y)</b>	60.87 ± 10.75	61.51 ± 9.92	0.749
<b>Liver function</b>			
TBIL (μmol/L)	342.82 ± 151.80	328.94 ± 140.95	0.624
DBIL (μmol/L)	274.36 ± 106.43	274.78 ± 116.25	0.984
AST (IU/L)	126.28 ± 118.43	172.20 ± 170.00	0.063
ALT (IU/L)	158.07 ± 148.84	178.86 ± 174.92	0.476
ALB (g/L)	37.03 ± 4.96	36.06 ± 6.56	0.330
<b>Blood routine</b>			
WBC (× 10 <sup>9</sup> /L)	7.14 ± 1.86	7.26 ± 2.18	0.744
HGB (g/L)	127.28 ± 16.73	123.17 ± 17.19	0.197
PLT (× 10 <sup>9</sup> /L)	297.92 ± 97.87	298.60 ± 84.33	0.970
<b>Coagulation function</b>			
PT (s)	12.82 ± 1.56	13.12 ± 1.37	0.290
APTT (s)	36.83 ± 4.59	37.13 ± 3.81	0.726
<b>Comorbidity</b>			
Diabetes	12 (8.4)	10 (28.6)	< 0.001 <sup>a</sup>
Gallstones in the gallbladder or bile ducts	9 (6.3)	8 (22.9)	0.003 <sup>a</sup>
<b>Obstruction location</b>			0.013 <sup>a</sup>
High-level obstruction	35 (24.5)	16 (45.7)	
Low-level obstruction	108 (75.5)	19 (54.3)	
<b>Types of malignant tumor</b>			0.998
Bile duct	74 (51.7)	18 (51.4)	
Pancreas	34 (23.8)	9 (25.8)	
Secondary	16 (11.2)	4 (11.4)	
Gallbladder	9 (6.3)	2 (5.7)	
Others	10 (7.0)	2 (5.7)	

Abbreviations: EBI, early biliary infection; TBIL, total bilirubin; DBIL, direct bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALB, albumin; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; PT, prothrombin time; APTT, activated partial thromboplastin time.

<sup>a</sup> Significantly different at P < 0.05.

drainage tube to control EBI. In cases of EBI, early administration of antibiotics is recommended. In our hospital, broad-spectrum antibiotics such as cefmetazole, cefoperazone-sulbactam, cefotiam, and piperacillin-tazobactam are used based on clinical experience until the results of drug sensitivity tests are available. Following the availability of sensitivity results, antibiotic therapy is adjusted accordingly. In cases where infection control is inadequate, and there is a tendency for worsening EBI, potent antibiotics like meropenem are employed. In this study, among 35 patients with EBI, appropriate anti-inflammatory treatment effectively controlled biliary infections.

### 3.3. Statistical Analysis

Statistical analysis was performed using SPSS 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Continuous data underwent normality assessment, and for normally distributed metric data, the independent *t*-test was applied, with results presented as mean ± standard deviation. Categorical data were presented as number (percentage), and those between two groups were compared by  $\chi^2$  test. This study classifies risk factors associated with EBI into two categories: Patient-related and surgical-related factors. Patient-related factors encompass sex, age, gallstones in the gallbladder or bile ducts, types of malignant tumor, obstruction location (low- or high-level), comorbidities (such as diabetes), preoperative liver function, blood routine, PT,

**Table 2.** Perioperative Parameters in Patients with and Without Early Biliary Infection<sup>a</sup>

Parameters	Non-EBI (n = 143)	EBI (n = 35)	P-value
Time from jaundice to <sup>125</sup> I stent implantation (days)	50.73 ± 31.03	45.49 ± 17.64	0.339
Time from PTBD to <sup>125</sup> I stent implantation (days)	22.55 ± 25.13	14.80 ± 16.89	0.009 <sup>b</sup>
Particle numbers	15.15 ± 4.62	15.26 ± 5.02	0.907
Intraoperative biliary bleeding	9 (6.3)	8 (22.9)	0.003 <sup>b</sup>
Drainage tube removal	97 (67.8)	22 (62.9)	0.575
Postoperative intrahepatic pneumobilia	53 (37.1)	22 (62.9)	0.006 <sup>b</sup>

Abbreviations: EBI, early biliary infection; PTBD, percutaneous transhepatic biliary drainage.

<sup>a</sup> Values are expressed as mean ± SD or No. (%).

<sup>b</sup> Significantly different at  $P < 0.05$ .

APTT, and postoperative intrahepatic pneumobilia. Surgical factors include <sup>125</sup>I particle numbers, intraoperative biliary bleeding, PTBD, time from PTBD to <sup>125</sup>I stent implantation (days), time from jaundice to <sup>125</sup>I stent implantation (days), and drainage tube removal. Observations are independent of each other. Univariate and multivariable logistic regression analyses were employed to identify independent risk factors influencing postoperative EBI, with those having  $P < 0.05$  subsequently subjected to multivariate logistic regression analysis to identify independent risk factors for EBI after <sup>125</sup>I particle stent placement. P-values less than 0.05 were considered statistically significant.

## 4. Results

### 4.1. Distribution of Bacterial Species in Early Biliary Infection

Within 30 days after implantation, EBI was observed in 35 patients (19.7%). The bacterial species in these patients were identified by bile culture, with positive results in all 35 cases. *Escherichia coli* (N = 17) was the dominant gram-negative bacterium in bile samples, followed by *Klebsiella pneumoniae* (N = 5), *Pseudomonas putida* (N = 3), and *Pseudomonas aeruginosa* (N = 1). Gram-positive bacteria included *Enterococcus faecalis* (N = 4) and *Staphylococcus* (N = 1). Additionally, mixed bacterial infections and *Candida* were identified in 3 and 1 cases, respectively.

### 4.2. Comparisons of Baseline Characteristics in Patients with and Without Early Biliary Infection

The baseline characteristics of patients with and without EBI were compared. As listed in Table 1, there were no significant differences in sex, age, liver function (TBIL, DBIL, AST, ALT, and ALB), blood routine (WBC, HGB,

and PLT), coagulation function (PT and APTT), and tumor types between the non-EBI and EBI groups. Notably, diabetes and gallstones (in the gallbladder or bile ducts) were more frequent in EBI cases compared to non-EBI cases ( $P < 0.01$ ). Patients with high-level obstruction were also more likely to suffer from EBI ( $P = 0.013$ ).

### 4.3. Comparisons of Perioperative Parameters in Patients with and Without Early Biliary Infection

The perioperative parameters were subsequently compared. The time from PTBD to <sup>125</sup>I stent implantation was significantly longer in non-EBI cases than in EBI cases ( $P = 0.009$ ). However, the time from jaundice to <sup>125</sup>I stent implantation and the number of particles were not significantly different between cases with and without EBI. Additionally, the removal of the drainage tube was not associated with the onset of EBI. Notably, intraoperative biliary bleeding and postoperative intrahepatic pneumobilia were more likely to be found in EBI cases compared to non-EBI cases ( $P < 0.01$ ) (Table 2).

### 4.4. Identification of Risk Factors for Early Biliary Infection

Based on the parameters with significant differences, multivariate logistic regression analysis was performed to determine the potential risk factors for EBI. As shown in Table 3, diabetes, gallstones in the gallbladder or bile ducts, high-level obstruction, intraoperative biliary bleeding, and postoperative intrahepatic pneumobilia were all identified as risk factors for EBI in patients who underwent <sup>125</sup>I particle stent implantation ( $P < 0.05$ ). Conversely, the time from PTBD to <sup>125</sup>I stent implantation was identified as a protective factor against EBI ( $P = 0.012$ ).

## 5. Discussion

Malignant biliary obstruction is an ominous disorder of biliary obstruction and cholestasis caused by the invasion of malignant tumors (14). Malignant biliary obstruction is accompanied by high mortality mainly due to tumor progression, liver failure, and sepsis (15). Percutaneous transhepatic biliary stenting, characterized by minimal invasion and high efficiency, is a common therapeutic strategy for MBO. The development of  $^{125}\text{I}$  particle stents brings great advantages in prolonging biliary patency and survival time (13). However, the onset of complications, including EBI, seriously affects the quality of life. In this study, EBI was observed in 35 patients (19.7%) after  $^{125}\text{I}$  stent implantation. Bile culture determined that the pathogens of EBI were mainly gut-derived bacteria, such as *E.coli*, *K.pneumoniae*, and *E.faecalis*. Additionally, several risk factors for EBI were identified, including diabetes, gallstones in the gallbladder or bile ducts, high-level obstruction, short time from PTBD to  $^{125}\text{I}$  stent implantation, intraoperative biliary bleeding, and postoperative intrahepatic pneumobilia.

Diabetes is a common metabolic disease characterized by hyperglycemia (16). Many previous studies have identified diabetes as a risk factor for EBI after PTBS (11, 13). In this study, diabetes was more frequent in the EBI group than in the non-EBI group and was subsequently determined to be a risk factor for EBI after  $^{125}\text{I}$  particle stent implantation. Our findings are consistent with previous studies, illustrating that diabetes is a risk for the onset of EBI following  $^{125}\text{I}$  particle stent implantation. The possible mechanisms include: (1) the reduction of insulin with anti-inflammatory effects (17); (2) weakened immune defense, leading to microbial invasion and infection (18); (3) diabetes-associated vascular disorders affecting blood flow around the bile duct, benefiting the growth of anaerobic bacteria under a hypoxic environment (19); and (4) hyperglycemia benefiting the growth of many bacteria in the bile duct (20). Therefore, preoperative control of blood glucose is urgently needed for patients requiring  $^{125}\text{I}$  particle stent implantation.

Gallstones grow inside the gallbladder or biliary tract, causing intermittent obstruction of the cystic duct (21). Gallstones can lead to a series of disorders, such as pain, jaundice, infection, and acute pancreatitis (22). A previous study reported that gallstones are a risk factor for cholecystitis within 30 days after PTBS (23). In this study, gallstones in the gallbladder or bile ducts were

determined to be a risk factor for EBI after  $^{125}\text{I}$  particle stent implantation. This result demonstrates the adverse role of gallstones in the outcomes of  $^{125}\text{I}$  stent implantation. The underlying mechanisms may be that gallstones can block the stent with the contraction of the gallbladder and the flow of bile, and the obstruction-induced cholestasis benefits bacterial growth, contributing to EBI. To avoid the adverse effects of gallstones, premature removal of PTBD drainage tubes is not recommended after stent implantation. When gallstones block the stent, they can be removed through the drainage tubes.

The location of obstruction is closely associated with the risk of biliary infection after drainage. Zhou et al. reported that the location of obstruction is a risk factor for EBI following PTBS (24). Consistent with previous studies, this study also revealed that high-level obstruction is a risk factor for EBI after  $^{125}\text{I}$  particle stent implantation. High-level biliary obstruction is characterized by an insidious onset and special anatomical location, which may lead to an increased risk of stent implantation and predispose to a variety of complications, such as EBI (25). For patients with high-level obstruction, accurate location of the obstruction based on preoperative cholangiography is necessary, and an appropriate stent should be customized to achieve sufficient drainage and reduce the risk of EBI.

Intraoperative biliary bleeding may occur due to mechanical damage caused by punctures, wire guides, and stents (26). Biliary bleeding can increase the risk of biliary infection by bringing contaminated bile into the bloodstream. Liu et al. reported that intraoperative biliary bleeding is an independent risk factor for EBI after PTBS (13). Consistently, this study also revealed that intraoperative biliary bleeding is a risk factor for EBI after  $^{125}\text{I}$  particle stent implantation. Therefore, avoiding vascular damage during interventional therapy is particularly important for reducing the risk of EBI.

Under normal circumstances, no gas is present in the bile duct. In this study, postoperative intrahepatic pneumobilia was observed in 75 cases after  $^{125}\text{I}$  particle stent implantation, which was more frequent in the EBI group than in the non-EBI group. The subsequent analysis determined a positive correlation between postoperative intrahepatic pneumobilia and EBI. The respiration of some bacteria contributing to EBI may lead to the onset of intrahepatic pneumobilia. After identifying bacterial gas in patients with postoperative intrahepatic pneumobilia, the drainage tube should be temporarily retained for flushing bile ducts.

**Table 3.** Multivariate Logistic Regression Analysis of Potential Risk Factors for Early Biliary Infection After I Particle Stent Implantation

Parameters	B-value	P-value <sup>a</sup>	OR	95% CI
Diabetes	1.203	0.029	3.329	1.129 - 9.819
Gallstones in the gallbladder or bile ducts	1.241	0.040	3.459	1.060 - 11.283
High obstruction	1.101	0.015	3.008	1.243 - 7.280
Intraoperative biliary bleeding	1.689	0.008	5.416	1.569 - 18.696
Postoperative intrahepatic pneumobilia	0.976	0.029	2.655	1.108 - 6.362
Time from PTBD to <sup>125</sup> I stent implantation	-0.035	0.012	0.966	0.940 - 0.992

Abbreviations: B, regression coefficient; OR, odds ratio; CI, confidence interval; PTBD, percutaneous transhepatic biliary drainage.

<sup>a</sup> Significantly different at P < 0.05.

The time from PTBD to <sup>125</sup>I implantation was further determined to be a protective factor for EBI. Patients with MBO usually have impaired immune function (27). Hyperbilirubinemia can further weaken cellular defense responses by stimulating cytotoxic reactions (28). Given that the normal protective barrier of the bile duct is easily damaged, interventional therapies, including PTBD, have a high risk of inducing biliary infection. Therefore, it is better to wait for the improvement of bilirubin, liver and coagulation function, and remission of edema in the bile duct wall before <sup>125</sup>I particle stent implantation. Our findings indicate that an appropriate extension of the time from PTBD to <sup>125</sup>I stent implantation is beneficial to reducing the risk of EBI.

In conclusion, patients with MBO have a relatively high incidence of EBI (19.7%) after <sup>125</sup>I particle stent implantation. Diabetes, gallstones in the gallbladder or bile ducts, high-level obstruction, intraoperative biliary bleeding, and postoperative intrahepatic pneumobilia are risk factors for EBI. The time from PTBD to <sup>125</sup>I stent implantation is a protective factor for EBI. However, this study is based on data from a single center with a limited sample size, potentially leading to biased results. The risk factors of EBI are not only limited to those elucidated in this study. Further research with a larger sample size and consideration of additional factors, such as the time of onset of malignancy, patient weight loss and malnutrition, and immunosuppression, is warranted.

### Supplementary Material

Supplementary material(s) is available [here](#) [To read supplementary materials, please refer to the journal website and open PDF/HTML].

### Footnotes

**Authors' Contributions:** F.S.: conceptualization, writing-original draft, funding acquisition and formal analysis; Y.N.: conceptualization, writing-original draft, and formal analysis; X.L.: investigation, validation, data curation; J.C.: validation, data curation, resources; H.H.: investigation, validation, data curation; Y.X.: conceptualization and writing-review & editing; M.H.: conceptualization and writing-review & editing; F.S. and Y.N. are co-first Author, these authors contributed equally to this work. All authors have read and approved the final manuscript.

**Conflict of Interests Statement:** The authors declare no conflict of interest.

**Data Availability:** The dataset presented in the study is available on request from the corresponding author during submission or after publication.

**Ethical Approval:** This study has received approval from the ethics committee of our hospital (ethical approval code, 2020-13) in accordance.

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