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Risk factors for biliary stent infections in malignant biliary obstruction secondary to unresectable malignancies

Sébastien Petit¹ · Mathieu Puyade² · Maxime Pichon^{1,3,4} · Marc Wangermez⁵ · Stéphane Velasco⁶ · France Roblot^{1,2,4} · Nicolas Isambert^{1,7} · Camille Evrard⁷ · Blandine Rammaert^{1,2,4}

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Abstract

Background Palliative biliary drainage in patients with unresectable malignant biliary obstruction (MBO) frequently leads to biliary stent infection (BI), which could impact medical care. The aim of this study was to assess the risk factors for BI occurrence in patients after stenting procedure and the impact of BI on patient survival.

Methods All consecutive patients hospitalized from 2014 to 2018 for MBO and biliary stenting were retrospectively included. Demographic, clinical, and microbiological characteristics of each BI episode during a 1-year follow-up were described. Documented BI was defined as the association of BI episode and confirmed blood stream infection (BSI). Univariate and multivariate analyses were performed to evaluate risk factors for the first BI occurrence.

Results Among 180 patients, 56% were men (mean age of 69±12), and 54% have pancreatic cancer, 16% biliary cancer, 2% hepatic cancer, and 28% lymph node or metastatic compression; metallic stent was placed in 92%. A total of 113 BI episodes occurred in 74 patients, 55% of the first episodes occurring within 3 months after stenting. BI was documented in 56% of the episodes. Enterobacteriaceae were the most frequent pathogens found, while no yeasts were documented. Mortality rate in patients with BI was 64%. Multivariate analysis showed a significant difference in BI occurrence for two criteria: WHO score 3–4 (OR=8.79 [1.79–42.89]; $p=0.007$) and transpapillary stenting location (OR=3.72 [1.33–10.44]; $p=0.013$).

Conclusion Since transpapillary stenting is a risk factor for BI, preserving the papilla as much as possible is a priority so as to avoid BI.

Keywords Cholangitis · Malignant biliary obstruction · Self-expandable metallic stents · Cancer · Biliary drainage · Transpapillary stenting

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Introduction

Pancreatic adenocarcinoma and cholangiocarcinoma are the two major cancers responsible for malignant bile duct obstruction (MBO). Nearly 70% of patients diagnosed with pancreatic adenocarcinoma have initial MBO and more than 80% of MBO is unresectable with a need for palliative drainage [1, 2]. MBO can also be due to metastatic pancreatic or hepatic cancer, ampullary tumors, gallbladder cancer, or malignant periportal lymph nodes [3]. The average survival of patients with pancreatic unresectable tumor is less than 1 year, around 11 months in published phase III studies [4, 5].

Biliary decompression in patients with unresectable MBO uses palliative biliary drainage. It is generally highly successful, safe, cost-effective, effective on pain control, and likely to improve the quality of life [6]. It can be achieved using different types of biliary stents, metallic uncovered,

partially covered, covered self-expandable (SEMS), or plastic stents (PS). Biliary stenting uses endoscopic or percutaneous approaches. The choice of appropriate endoscopic or percutaneous procedure and stent for palliative MBO often results in complex multidisciplinary team discussions.

Complications may occur during or after the stenting procedure. Early complications such as pancreatitis, cholangitis, and sepsis are secondary to both endoscopic and percutaneous approaches [7–15]. Long-term complications may be related to type of stent, tissue overgrowth, and bacterial/fungal environment; stent obstruction, stent migration, and biliary stent infection (BI) are the three main complications [7, 16–24]. While stent obstruction and migration have been reported in many studies, only a few of them have described BI, with rates ranging from 10 to 30% [16–18, 20, 22]. In addition, studies have focused on only one type of procedure or stent.

Choice of stenting approaches, type of stent, or patient characteristics could influence the onset of BI. The aim of this study was consequently to assess risk factors for a first BI in patients with cancer treated by palliative biliary stent.

Material and methods

Design

This French retrospective observational bicentric study was conducted at the Poitiers University Hospital, a 1900-bed tertiary care hospital, and at La Rochelle Hospital, a 1700-bed secondary care hospital. From January 1, 2014, to December 31, 2018, all consecutive patients over 18 years old with MBO who needed biliary stenting through endoscopic or percutaneous approach were included. All BIs were noted and patients were followed for 1 year after stenting.

Patients with lack of information, prior biliary stenting, stent removal, healthcare-associated liver abscess developing within a month following stenting procedure, or surgical revision before the end of supervision were excluded.

Ethics

The National Data Protection Authority (Commission Nationale Informatique et Libertés), which is responsible for the protection of individual data in France, approved the study (registration number CHU86-R2019-10-03).

Data collection

Patients were selected through the stenting register of each hospital. After having checked inclusion and exclusion criteria, data were collected on the day of stenting and included

the following: age, sex, type of cancer, concomitant use of chemotherapies, WHO score performance status, TNM classification, nutritional status (estimated by albuminemia and proteinemia), body mass index (BMI) at stenting, date and type of stenting procedure, stent material (plastic or metallic), need for sphincterotomy or external drainage during the procedure, stenosis localization (intra-pancreatic, between the pancreas and liver, or intra-hepatic), stenting localization (across or above the main duodenal papilla), infection within the last 3 months before the procedure, use of antibiotic prophylaxis or therapy, post-procedure infection complications other than BI, diabetes, renal insufficiency, and intake of corticosteroids or proton pump inhibitors. For each BI episode, the number of lines of chemotherapy used, albuminemia, proteinemia, BMI, intake of corticosteroids, bloodstream infection (BSI), appropriateness of antibiotic therapy at the onset of infection and after 48 hours, and patient death occurring during 1-year medical supervision were reported.

Of note, at our institutions, there are no written antibiotic therapy protocols to treat patients suspected for BI. A broad-spectrum beta-lactam such as piperacillin-tazobactam combined with vancomycin in the case of early post-stenting infection is usually used. In the other cases, patients receive third-generation cephalosporin combined with metronidazole or amoxicillin-clavulanic acid even when they are undergoing chemotherapy and have frequent hospital stays. Amikacin is added in the case of sepsis or septic choc.

Definition

Currently, no standard definition of BI is globally admitted. As the definition should consider previous biological disorders due to cancers and chemotherapies, the selected criteria were adapted from Tokyo Guidelines 2018, which took into account patients' previous biological disorders [25]. BI was defined as fever $\geq 38.3^{\circ}\text{C}$ without other infections suspected; both transaminases > 3 times the upper limit of normal (ULN) or > 1.5 times the patient's average level in previous blood tests if transaminases were already 3 times ULN; alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) > 1.5 times ULN; and an increase in CRP ULN or > 1.5 times the patient's average level if CRP was higher before BI episode (Table 1).

Documented BI was defined as the association of BI episode and confirmed BSI. BSI was defined according to the National Healthcare Safety Network [26]. In our institution, all patient's files with positive blood cultures were reviewed by a senior infectious disease specialist so as to eliminate contamination. All patients with fever $\geq 38.3^{\circ}\text{C}$ or chills or sepsis signs or hypothermia had at least two sets of aerobic and anaerobic blood cultures. A blood culture was considered to be contaminated if one or more of the following

Table 1 Proposed definitions of biliary stent infections (BI)

BI	<ul style="list-style-type: none"> • Fever $\geq 38.3^{\circ}\text{C}$ without other infections suspected • AND both transaminases $> 3 \times \text{ULN}$ or $> 1.5 \times$ the patient's average level in previous blood tests if transaminases were already $3 \times \text{ULN}$ • AND ALP and GGT $> 1.5 \times \text{ULN}$ • AND increase in CRP ULN or $> 1.5 \times$ the patient average level if CRP was higher before BI episode
Documented BI	BI AND bloodstream infection
Severe BI	BI AND sepsis or septic choc

ULN, upper limit of normal; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; CRP, C-reactive protein; BI, biliary stent infection

organisms were identified in only one of a series of blood culture specimens: coagulase-negative *Staphylococcus* spp., *Cutibacterium acnes*, *Micrococcus* spp., “viridans”-group streptococci, *Corynebacterium* spp., or *Bacillus* spp. A blood culture series was defined as one or more specimens collected serially within a 24-h period to detect a bacteremic episode [27].

Severe BI was described as the association of BI episode with sepsis or septic shock defined according to The Surviving Sepsis Campaign Definitions for Sepsis and Septic Shock [28].

Death was considered attributable to BI if it occurred during the BI episode.

Renal failure was defined by plasma creatinine clearance according to MDRD ≤ 30 ml/min/1.75 m².

Corticosteroids were considered if equivalent prednisolone dosage was > 10 mg/day for more than 9 weeks or > 700 mg in cumulative dose. Corticosteroids included in chemotherapy protocol were not taken into account [29].

Current first-line treatment of non-severe BI in our two institutions is a combination of third-generation cephalosporin and metronidazole as recommended by Tokyo Guideline 2013 and 2018 for acute cholangitis [25, 30]. Another antibiotic regimen can be used at the discretion of the clinician. For this reason, the antibiotic therapy used in documented BI was described in view of determining its appropriateness. Antibiotic regimen was considered appropriate if both good tissue diffusion and in vitro antimicrobial activity were achieved [31].

Statistical analysis

Quantitative variables were described as mean \pm standard deviation (SD) in the case of normal distribution or median and interquartile range (IQR 25–75) otherwise. Comparisons were performed depending on the situation with Student's *t* test or with the non-parametric Mann-Whitney test. Qualitative variables were described as percentages with confidence intervals, compared with the chi-square test. Due to the low

rate of survival at 1 year, survival was considered a binomial variable. To establish the factor associated with BI (binary variable), logistic regression was performed. Univariate analysis was conducted to select variables with *p* value < 0.2 to be further analyzed in the multivariate analysis. Bivariate analysis was performed with clinically relevant interaction. Multivariate analysis was conducted with a backward stepwise method (*p* < 0.05). Only confounding factors and factors with a significant *p* < 0.05 were conserved in the final model. Model fit regression was assessed with the Hosmer-Lemeshow goodness of fit test. A *p* value below 0.05 was considered significant.

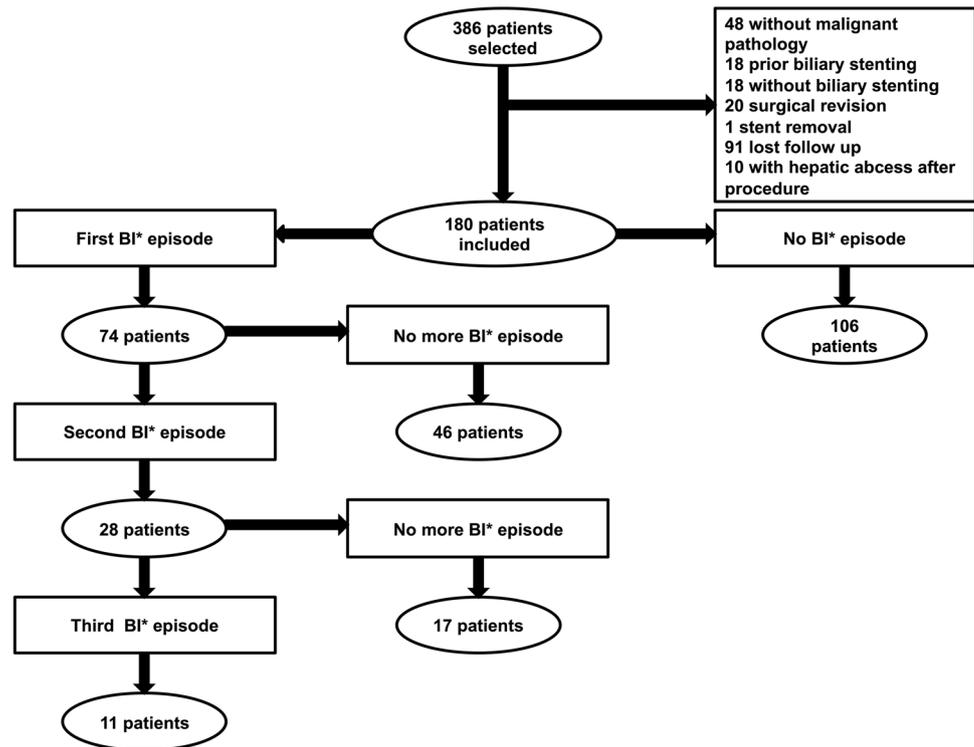
Results

Population characteristics

Among 386 adult patients with stenting procedure, 180 (47%) were included. The flowchart of the study is represented in Fig. 1. Demographic characteristics of the patients at stenting procedure are shown in Table 2. The majority of patients were men (101/180; 56%) with a mean age of 69 ± 12 years at stenting. In more than half of the cases, the primary cancer was pancreatic (99/180; 55%) and it was metastatic (97/174; 56%). Severe hypoalbuminemia < 30 g/L was detected in 56/162 (35%) patients. The endoscopic procedure was used for 139 (139/180; 77%) patients. All patients who underwent percutaneous procedure received an antibiotic prophylaxis. Prophylaxis was given to one patient for endoscopic procedure. Metallic stents were the most widely used (166/180; 92%). Stents were uncovered (*n*=90; 50%), partially covered (*n*=1; 1%), or covered (*n*=36; 20%), or covering was unknown (*n*=39; 21%).

A total of 74 (41%) patients suffered a first BI during the year after stenting; only two had concomitant neutropenia. During the follow-up, 46 (62%) had only one BI episode, 17 (23%) presented two BIs, and eleven (15%) presented three BIs. Mean time between stenting and the first BI was $112 \pm$

Fig. 1 Flowchart of the study.
*BI, biliary stent infection



108 days. In the first month after stenting, the rate of patients with a first BI was high (22/74; 30%), and decreased gradually each month (Fig. 2). Consequently, 41 patients (55%) had a BI during the first trimester, while only 19 patients (26%) had a first BI episode during the last 6 months of monitoring. Chemotherapy was administered in 54 patients (30%) before stenting procedure; among them, 19 (35%) presented a BI during the follow-up.

The mortality rate was high (110/180; 61%) at 1 year for the global cohort (Fig. 3). The mortality rate of patients with BI (47/74; 64%) did not differ according to the number of BI recurrences with 32 out of 46 (70%), 7 out of 17 (41%), and 8 out of 11 (72%) patients who presented one, two, and three BIs, respectively ($p=0.10$). Death was attributable to BI in 11 out of the 47 patients (23%).

BI episode characteristics

A total of 113 BI episodes were then studied, 14 episodes (12%) being considered severe, necessitating admission in an intensive care unit. Chemotherapy was ongoing for 71 (63%) BI episodes. Biliary reintervention was performed in 7 patients in the first 48 h of the first BI diagnosis: in one patient, a plastic stent was removed and replaced by a metallic stent, and in 6 patients a metallic stent was added to the one still in place. Bile culture was not routinely performed in these cases. All 7 patients had received at least one dose of antibiotic before intervention.

Documented BI with positive blood culture represented 62 (55%) episodes (Fig. 4). Monomicrobial infections were found in 74% (46/62) of the documented infections.

Gram-negative bacilli (GNB) represented most of the bacteria (37/46; 80%) found in blood cultures of monomicrobial infections. The three main GNB were *E. coli* ($n=22$), *Enterobacter* spp. ($n=5$), and *Klebsiella* spp. ($n=3$). Regarding Gram-positive cocci (GPC) (9/46; 20%), the main pathogens were *Enterococcus* spp. ($n=5$) and *Streptococcus* spp. ($n=3$). No Gram-positive bacilli or yeasts were found. Distribution of bacteria species between mono- and polymicrobial BI, and between the first BI episode and the other episodes could not be considered significantly different ($p>0.05$) (Supplemental Table 1).

Among the 62 documented BIs, 61 received empirical first-line antibiotic therapy, while one patient directly received targeted antibiotics after waiting for blood culture results at the discretion of the clinician (Supplemental Table 2).

The majority of the non-severe documented BIs were treated using a first-line empirical combination of two antibiotics (39/47; 83%), mostly third-generation cephalosporin and metronidazole (34/39; 87%). The combination was appropriate in 33 (33/39; 85%) non-severe documented BI episodes. Among the six patients who presented pathogens resistant to the initial empirical antibiotic regimen, five had polymicrobial infections and one died less than 48 h after BI diagnosis. A total of eight episodes (8/47; 17%) were

Table 2 Baseline characteristics of 180 patients with malignant biliary obstruction at stenting procedure

Characteristics	Overall population, <i>N</i> = 180	Patients with BI, <i>n</i> = 74	Patients without BI, <i>n</i> = 106
Age at procedure (years), mean ± SD	69 ± 12	67 ± 12	70 ± 11
Male gender	101 (56)	45 (61)	56 (53)
BMI (kg/m ²), mean ± SD ^{&}	25 ± 5 [158]	25 ± 4 [67]	25 ± 6 [91]
Proteinemia (g/L), mean ± SD ^{&}	62 ± 9 [168]	63 ± 9 [68]	61 ± 9 [100]
Albuminemia (g/L), mean ± SD ^{&}	32 ± 6 [162]	33 ± 6 [68]	33 ± 6 [94]
Diabetes	43 (24)	21 (28)	22 (21)
Renal insufficiency	6 (3)	2 (3)	4 (4)
Splenectomy	2 (1)	2 (3)	0 (0)
Corticosteroids	17 (9)	6 (8)	11 (10)
Proton pump inhibitors	45 (25)	17 (23)	28 (26)
Infection in the previous 3 months before stenting	16 (9)	3 (4)	13 (12)
Type of cancer			
Pancreatic	99 (55)	36 (49)	63 (59)
Biliary	28 (16)	17 (23)	11 (10)
Hepatic	3 (2)	1 (1)	2 (2)
Other primitive cancer *	50(28)	20 (27)	30 (28)
Stage of TNM classification [‡]			
I	19/174 (10)	8/73 (11)	11/101 (11)
II	22/174 (13)	6/73 (8)	16/101 (16)
III	36/174 (21)	14/73 (19)	22/101 (22)
IV	97/174 (56)	45/73 (62)	52/101 (51)
Chemotherapy			
No chemotherapy	115	51	64
1st line	25	9	16
2nd line	20	5	15
≥ 3rd line	20	9	11
Biliary stenosis localization			
Pancreatic	123 (68)	42 (57)	81 (76)
Between pancreas and liver	21 (12)	13 (18)	8 (8)
Liver	20 (11)	10 (13)	10 (9)
≥ 2 localizations	16 (9)	9 (12)	7 (7)
Procedure used			
Percutaneous	41 (23)	18 (24)	23 (22)
Endoscopic with sphincterotomy	110 (61)	47 (64)	63 (59)
Endoscopic without sphincterotomy	29 (16)	9 (12)	20 (19)
Type of stent			
Plastic	14 (8)	9 (12)	5 (5)
Metallic **	166 (92)	65 (88)	101 (95)
Transpapillary stenting [§]	143/166 (86)	51/64 (77)	92/102 (90)
Presence of external drain	25 (14)	12 (16)	13 (12)

All variables are expressed in absolute number with percentage (%), otherwise indicated

[&]Some data are missing for these categories. The total number of collected values is indicated in italic into brackets

*Lymph node or metastatic compression due to lung, breast, stomach, and/or colon cancers

**Uncovered (*n*=90; 50%), partially covered (*n*=1; 1%), covered (*n*=36; 20%), unknown (*n*=39; 21%)

[‡]Unknown TNM classification for 6 patients

[§]Unknown for 14 patients

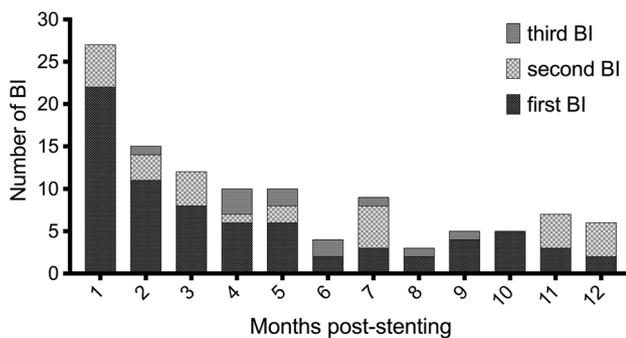


Fig. 2 Distribution of biliary stent infection (BI) episodes over a 1-year surveillance period

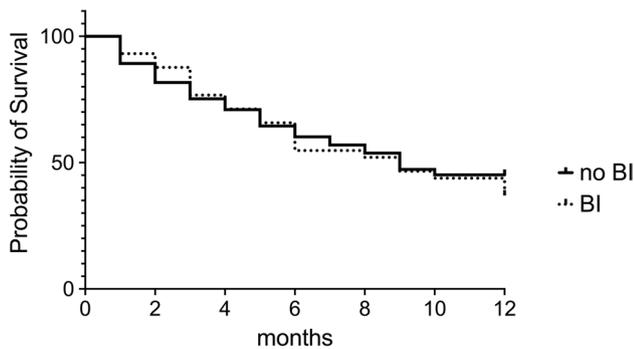
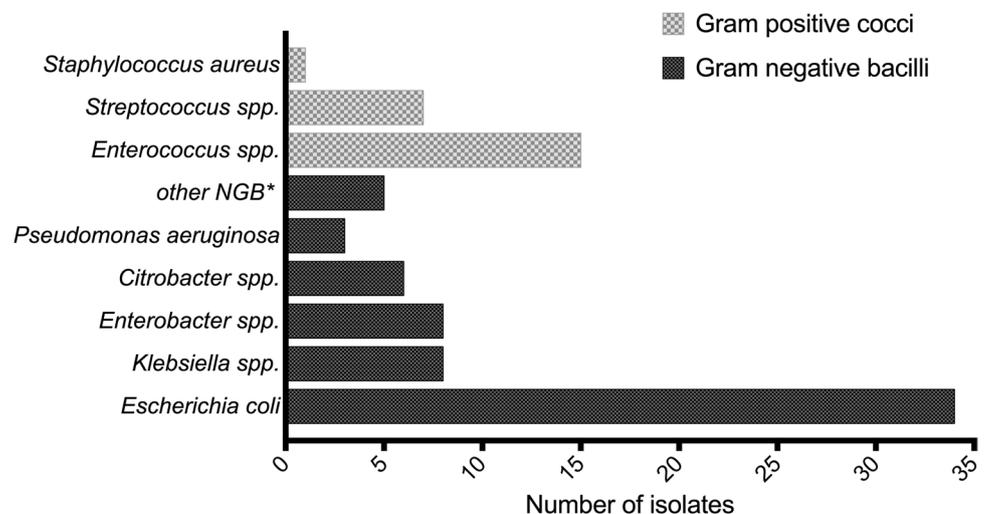


Fig. 3 Survival curve for 180 patients with or without biliary stent infection (BI) episodes

treated with one antibiotic alone, which was appropriate in six episodes (6/8; 75%); unlike amoxicillin-clavulanate and ceftriaxone, which were appropriate in all six cases, none of the amoxicillin-alone therapies was appropriate.

For severe documented BI, piperacillin-tazobactam was used alone in five episodes (5/14; 36%) and was appropriate

Fig. 4 Distribution of bacteria responsible for 62 episodes of documented biliary stent infection (BI). **Serratia marcescens*, *Stenotrophomonas maltophilia*, *Haemophilus parahaemolyticus*, *Hafnia alvei*



in four (4/5; 80%). The combination of two or more antibiotics was always appropriate in all the other episodes (9/9; 100%).

Death was attributable to BI for 11 (11/113; 10%) episodes, 7 (64%) being documented. Among them, two had received an appropriate antibiotic.

Risk factors for BI

Univariate and multivariate analyses of risk factors leading to at least one BI episode are presented in Supplemental Table 3 and Table 3, respectively. In multivariate analysis, two factors were significantly associated with the occurrence of at least one BI: transpapillary stenting and WHO performance status 3–4 after adjustment on the type of cancer (confounding factor). In addition, a first BI episode could not be considered a risk factor for another BI episode, and a first BI episode was not associated with change in survival ($p > 0.05$).

Discussion

To the best of our knowledge, this study was the first to propose a BI definition for MBO adapted to previous biological disturbances. It showed that transpapillary stenting and alteration of health status measured through WHO performance status > 2 were associated with the occurrence of a first BI. The different procedure approaches, stents used, localization of stenosis, characteristics of patients, stage of cancer, or a prior BI did not precipitate a BI episode. Moreover, BI did not impact patient survival even if mortality attributable to BI remained high.

WHO performance status is known to be associated with an increased risk of infections in patients with cancer and neutropenia but not with BI in MBO [32]. Risk factors for

Table 3 Multivariate analysis of risk factors for biliary stent infection

Variables	Multivariate analysis	
	OR CI95	<i>p</i> value
WHO performance status		
0–2	ref	
3–4	8.79 [1.79–42.89]	0.007
Transpapillary stenting	3.72 [1.33–10.44]	0.013

early BI within 1 month after the stenting procedure have been studied in two recent publications with heterogeneous populations. Tierney et al. studied 431 patients including 65 with cancer. They showed that low serum albuminemia, multiple stents, primary cancer diagnosis, and high level of transaminases and alkaline phosphatase were risk factors for early BI after endoscopic retrograde cholangiopancreatography (ERCP) [33]. Xu et al. demonstrated that proton pump inhibitor use, diabetes, and biliary stones were risk factors for early BI in 134 patients with unresectable MBO undergoing percutaneous procedure [34]. These studies did not take into account stenosis and stent localization.

Our study integrated these two parameters and showed that stent localization was a significant risk factor for the occurrence of at least one episode of BI. Two other studies have analyzed the incidence of BI linked to stent localization. Huang et al. showed that the incidence of BI with transpapillary stenting was significantly higher than above the papilla in 98 patients with MBO undergoing percutaneous procedure with metallic stents [35]. Okamoto et al. demonstrated the significant influence of transpapillary stenting on BI occurrence in 108 patients with MBO using metallic stents and undergoing percutaneous or ERCP procedure [36]. Another study had contradictory results, finding no relation between stenting localization and occurrence of BI in 100 patients undergoing mostly ERCP with uncovered metallic stent [37]. Jo et al. obtained the same results in 155 patients undergoing percutaneous procedure [38]. However, transpapillary stenting was associated with a significant difference in occurrence of pancreatitis and complications in general. The loss of papilla functionality may enhance duodeno-biliary reflux. Preserving the papilla or using antireflux metal stent when the stent is transpapillary could overcome this issue. However, antireflux metal stents are still under investigation and randomized control trials did not show differences in BI occurrence [39].

In contrast to ERCP guidelines, the Society of Interventional Radiology has recommended antibiotic prophylaxis before the percutaneous stenting procedure, even if there is no consensus on the choice of antibiotic [40, 41]. Although 100% of our patients received antibiotic prophylaxis before percutaneous stenting, no significant difference was found between the two procedures as risk factors for

BI. Prophylaxis may have lowered the incidence of BI in the case of percutaneous stenting.

In our study, we postulated that the bacteria found in blood cultures were from stent biofilm and were representative of BI. However, the distribution of microorganisms between blood and bile culture seems different. To the best of our knowledge, since metallic stent cannot be retrieved, biliary stent colonization has been studied only on plastic stents retrieved after variable time. Lübbert et al. studied microorganisms from biofilm of plastic stents retrieved after median indwelling time of 63 days [42]. Enterobacteriaceae, *Enterococcus* spp., and *Candida* spp. were the leading pathogens found when culturing these samples. The same microorganisms were found in another study that observed a change in microbial colonization of the stents with indwelling time [43]. One study addressed the issue of correlation between bile and blood cultures in 90 patients with MBO necessitating external biliary drainage without any biliary stent [44]. More than half of the patients (48/90; 53%) had positive blood cultures, of whom 29 (29/48; 60%) also had positive bile culture. The distribution of pathogens was completely different between bile and blood cultures for 62% of the patients with predominance of GPC over GNB in bile culture. Another study describing the distribution of pathogens from biliary external drainage culture also found a predominance of GPC (50.9%) over GNB (41.5%) (yeasts representing 7.5% of the pathogens) [45]. Enterobacteriaceae were responsible for 80% of the monomicrobial BI episodes in our study. Bile culture was not routinely performed in our centers in the setting of reintervention on the biliary duct, and most of the patients did not have external drainage at the time of BI. Of note, this routine of not using the microbiological data from the bile is specific to our institutions. In addition, positive bile culture is not taken into account when choosing antibiotic therapy, as it may represent metallic stent colonization rather than biliary stent infection decapitated by prior antibiotic therapy.

In the present study, mortality rate attributable to BI was high (10%), and was partially due to failure of initial antibiotic therapy. The combination of third-generation cephalosporin and metronidazole was ineffective against 15% of the digestive pathogens in monomicrobial non-severe BI due to bacterial resistance. In the case of severe BI, the combination of wide-spectrum beta-lactams and glycol-/lipo-peptides active against GPC had a high success rate.

Since 35% of our patients had severe hypoalbuminemia, it may impact antibiotic pharmacokinetics, thereby compromising the attainment of pharmacodynamic targets. Indeed, hypoalbuminemia increases the unbound fraction of the drug and is responsible for larger volume of distribution and clearance from the plasma to the peripheral compartment. These changes reduce antibiotic exposure and blood concentrations, especially for antibiotics with

high protein binding such as third-generation cephalosporins [46]. To ensure better efficacy, antibiotic dosage must be corrected according to the albuminemia concentration [47]. A combination of antibiotics including GNB and GPC in their spectrum is consequently mandatory in the case of severe BI and should be discussed in patients with non-severe BI, depending on local epidemiology.

The present study had some limitations, mostly due to its retrospective nature and the absence of consensual diagnosis criteria for BI. Herein, the diagnosis criteria for BI were adapted from Tokyo Guideline 2018 on cholangitis diagnosis [25]. BI diagnosis criteria should consider clinical and biological disorders associated with biliary infection and abnormalities caused by cancer and therapeutics. Considering patients' baseline biological results before infection was one way to overcome these constraints. Regarding clinical symptoms, abdominal pain was usually unspecific to infection since patients had digestive cancer and were receiving strong analgesics. The radiological diagnosis criteria remain relevant on cholangitis diagnosis in association with clinical and biological criteria without any studies having evaluated performances (sensitivity and specificity) in biliary stent infection [25]. In our centers, it is not common practice to perform abdominal ultrasonography or computerized tomography in the case of BI suspicion since interpretation in the context of MBO remains difficult and is limited to symptom worsening or lack of response to antibiotic therapy. For reasons of significance, the type of chemotherapy used was not analyzed in this study.

The "intake of corticosteroid" criterion did not consider corticosteroids used in chemotherapy due to lack of access to data regarding the corticosteroids included in chemotherapy. Corticosteroids included in chemotherapy protocols could have influenced BI occurrence. In this study, chemotherapy was administered in one-third of the patients (54/180) before stenting procedure leading to BI in 19 (35%) cases.

Definition accuracy of attributable death could be questionable. Death was considered attributable to BI if it occurred during the BI episode. However, the cause of death is difficult to determine between the BI episode and the progression of cancer.

To conclude, localization of biliary stent and poor general status may influence occurrence of a first BI. Preserving the papilla functionality as much as possible is a priority to avoid BI while waiting for further improvements in antireflux stents. There is also an urgent need to have a consensual definition of BI in the context of MBO and to implement specific recommendations for BI management.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00520-022-07106-2>.

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Author contribution SP, BR, and MP conceived and designed the study; SP, MW, SV, CE, and MPi collected the data; SP, BR, MP, MPi, FR, NI, and CE contributed to analysis and interpretation of data; SP, BR, and MP performed the analysis; all authors contributed to manuscript preparation, reviewed the results, and approved the final version of the manuscript.

Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics approval The National Data Protection Authority (Commission Nationale Informatique et Libertés), which is responsible for the protection of individual data in France, approved the study. The protocol was registered as CHU86-R2019-10-03.

Consent to participate Since French law does not require written informed consent for retrospective studies, all individual participants alive at the time of the study were informed of the study and were asked for their permission to collect and utilize their individual data.

Consent for publication Not applicable.

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