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ORIGINAL ARTICLE

Risk Factors for Cholangitis After Pancreatoduodenectomy: A Systematic Review

Youcef Salaheddine[1] · Anne Claire Henry[1] · Lois A. Daamen[1] · Wouter J. M. Derksen[1] · Krijn P. van Lienden[2] · I. Quintus Molenaar[1] · Hjalmar C. van Santvoort[1] · Frank P. Vleggaar[3] · Robert C. Verdonk[4]

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Abstract

Background Cholangitis is a late complication after pancreatoduodenectomy with considerable clinical impact and is difficult to treat. The aim of this systematic review was to provide an overview of the literature identifying risk factors for postoperative cholangitis.

Methods A systematic search of the databases PUBMED and EMBASE was performed to identify all studies reporting on possible risk factors for cholangitis following pancreatoduodenectomy. Data on patient, peri- and postoperative characteristics were collected. Risk of bias assessment was done according to the methodological index for non-randomized studies (MINORS) criteria.

Results In total, 464 studies were identified. Eight studies met the inclusion criteria for this analysis. The definition of postoperative cholangitis was inconsistent, with four studies using the Tokyo Guidelines, whereas other studies used different definitions. Data on 26 potential risk factors concerning the patient, peri- and postoperative characteristics were analyzed. Five factors were significantly associated with cholangitis in two or more studies: high body mass index, duration of surgery, benign disease, postoperative pancreatic fistula, and postoperative serum alkaline phosphatase.

Conclusion Multiple potential risk factors for postoperative cholangitis were identified, with large discrepancies between studies. Prospective research, with consensus on the definition, is required to determine the true relevance of these risk factors.

Keywords Pancreatoduodenectomy · Cholangitis · Hepaticojejunostomy · Risk factor

Introduction

Pancreatoduodenectomy is a challenging surgical procedure with a high risk of short-term complications [1]. Even though the 30-day mortality rate has decreased to less than 3%, morbidity remains high at around 45% [2, 3]. Common complications include postoperative pancreatic fistula, bile leakage, and delayed gastric emptying [2, 3]. A serious long-term complication that is less studied, but can have severe clinical impact, is postoperative cholangitis. The previously reported incidence is approximately 10% [4]. Postoperative cholangitis may occur in combination with an anastomotic or intrahepatic biliary stricture, but can also be caused in absence of an obstruction, by colonization of bacteria from the intestines up the biliary tree [5–7]. This colonization, resulting in ascending cholangitis, is possible due to the absence of the sphincter of Oddi after pancreatoduodenectomy, which has a barrier function [8].

✉ Robert C. Verdonk
r.verdonk@antoniusziekenhuis.nl

Youcef Salaheddine
y.salaheddine@students.uu.nl

1 Department of Surgery, Regional Academic Cancer Center Utrecht, St. Antonius Hospital Nieuwegein, University Medical Center Utrecht, Utrecht, The Netherlands

2 Department of Radiology, Regional Academic Cancer Center Utrecht, St. Antonius Hospital Nieuwegein, University Medical Center Utrecht, Utrecht, The Netherlands

3 Department of Gastroenterology & Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands

4 Department of Gastroenterology & Hepatology, Regional Academic Cancer Center Utrecht, St. Antonius Hospital Nieuwegein, University Medical Center Utrecht, Koekoekslaan 1, 3435 CM Nieuwegein, The Netherlands

Little is known about the risk factors for cholangitis after pancreatoduodenectomy. Studies that have been done, often have conflicting results. This can be partly explained by the absence of clear definitions for cholangitis after pancreatoduodenectomy. Acute cholangitis in patients without previous pancreaticobiliary surgery can be diagnosed according to the Tokyo Guidelines 2013 (TG13) [9]. Although these consensus definitions are far from perfect, they facilitate research and comparison between studies [10]. For diagnosing acute cholangitis, these guidelines state that signs of systemic inflammation, cholestasis, and radiologic imaging with either biliary dilatation or evidence of an identifiable cause (e.g., stricture and stone) should be present [11–13]. Ascending cholangitis can, however, also occur in the absence of an identifiable cause. Therefore, these guidelines may not be suitable for patients who underwent pancreatoduodenectomy.

The aim of the current systematic literature review was to identify risk factors for postoperative cholangitis to improve the understanding of this potentially severe complication.

Materials and Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [14].

Search Strategy and Eligibility Criteria

A systematic literature search of the databases PubMed, Embase, and Cochrane Library from January 1, 2000 to June 14, 2021 was conducted. The search terms were medical subject headings (MeSH) terms and synonyms for 'pancreatoduodenectomy' in combination with 'cholangitis' (Supplementary Table 1).

Inclusion criteria were studies reporting on (1) patients who underwent a pancreatoduodenectomy and (2) presenting data on the incidence of postoperative cholangitis and potential risk factors. Exclusion criteria were as follows: (1) animal studies, (2) studies including less than 10 patients with cholangitis, (3) studies including surgical procedures other than pancreatoduodenectomy, (4) studies including patients with primary sclerosing cholangitis, (5) no full text available, and (6) non-English articles.

Study Selection and Data Extraction

All studies obtained from the literature search were exported to Rayyan for duplicate and relevance screening [15]. Removal of duplicates, screening of titles and abstracts and full text screening was performed by YS and ACH independently, using the pre-specified eligibility criteria. In case of disagreement, a third author was consulted (LD). Cross-reference checking of included full-text articles was performed to identify potential relevant studies that were missed during the initial literature search.

Quality Appraisal

The included articles were assessed for risk of bias by two authors (YS, ACH), using the revised and validated version of the 'Methodological Index for Non-Randomized Studies' (MINORS) checklist [16]. A total of seven items were selected for bias screening. Each item was assessed as 0 (not reported), 1 (reported but suboptimal), or 2 (reported and adequate). This resulted in a minimum score of 0 and a maximum score of 14. The study aim was deemed suboptimal if it differed substantially from the aim of this systematic review. If criteria for inclusion and exclusion were dissatisfying or missing, representativeness of the study population was considered suboptimal. Reporting of relevant determinants was insufficient, if data regarding patient characteristics and peri- and postoperative details were poorly presented. A clear and adequate definition of the outcome required details regarding the diagnostic criteria. Analysis of study outcomes was deemed suboptimal if patients with cholangitis were analyzed in combination with patients experiencing other biliary complications, and results were not separately presented. The follow-up period was insufficient in case of a median postoperative follow-up of less than 12 months. Lost to follow up was considered to cause bias if the 5% threshold was exceeded [17].

Data Analysis

The following data were extracted from the included articles by YS: date of publication, study design, sample size, definition of postoperative cholangitis, incidence of postoperative cholangitis, patient characteristics, and perioperative and postoperative details. Descriptive statistics were presented as in the original article. Continuous variables were presented as mean ± standard deviation (SD) or median (range). Categorical variables were presented as number and percentages. If available, odds ratios (OR) with 95% confidence interval (95% CI) and *P* values were included. When possible, subgroup analysis was conducted with Review Manager (RevMan) for studies that had comparative outcome measures [18].

Results

A total of 535 studies were identified (Fig. 1). After removing duplicates and title/abstract screening, 37 original full texts were assessed for eligibility. In total, eight studies were

Fig. 1 PRISMA flow chart

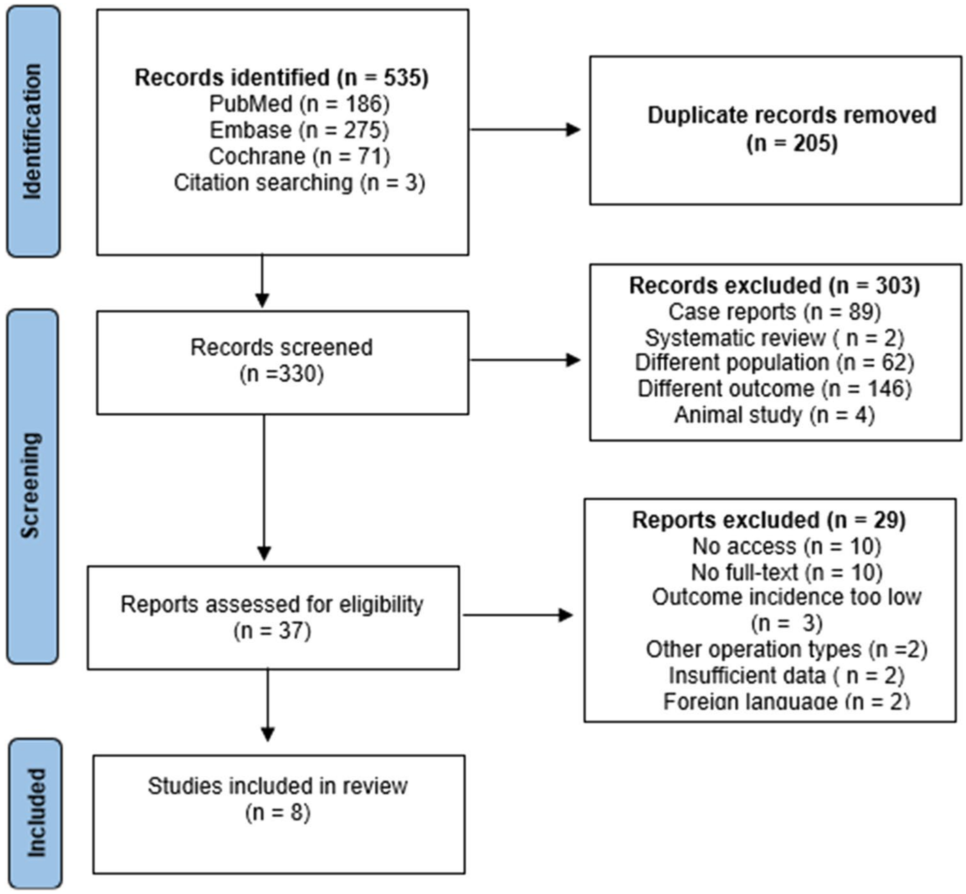

Table 1 Study characteristics

References	Study design	Year	Study period	Patients	Outcome	Postoperative cholangitis (%)	Risk of bias
Brown and Zenati [18]	RS	2020	2010–2017	628	Biliary stricture, cholangitis, and pancreatitis	50 (8)	13/14
Brown and Jung [19]	RS	2020	2011–2018	241	Cholangitis or stricture	27 (11,2)	8/14
Ito [20]	RS	2018	2007–2016	133	Cholangitis	28 (21,1)	11/14
Ueda [21]	RS	2017	2007–2013	113	Recurrent cholangitis	21 (18,9)	10/14
Asano [22]	RS	2016	2008–2013	213	Cholangitis with HJ stenosis	16 (8,1)	9/14
Hiyoshi [23]	RS	2016	2002–2010	161	Cholangitis	13 (8,1)	10/14
Malgras [24]	RS	2016	2007–2011	352	Cholangitis	20 (6)	9/14
Parra-Membrives [25]	RS	2016	2001–2014	86	Recurrent cholangitis	14 (16,3)	10/14

RS retrospective study, *HJ* hepaticojejunostomy

included and critically appraised (Supplementary Table 2) [19–26]. Study characteristics are presented in Table 1.

The eight included studies were all retrospective cohort studies, reporting on a total of 1927 postoperative patients, of whom 189 patients developed postoperative cholangitis (10%). Incidence of postoperative cholangitis ranged from 6 to 21% [21, 25]. Four studies studied cholangitis as the main outcome [21, 24–26]. Two studies included only patients that had recurrent cholangitis, which occurred in 16% and 19% of the patients [22, 26]. Alternatively, one study combined cholangitis or biliary stricture as the main outcome, while another study focused on either biliary stricture, cholangitis or pancreatitis [19, 20]. Furthermore, one study reported on cholangitis with hepaticojejunostomy stenosis as the main outcome [23].

Patient, Peri- and Postoperative Characteristics

Table 2 presents all patient characteristics that were studied as potential risk factors. A higher body mass index (BMI) was the only patient characteristic that was a significant risk factor of postoperative cholangitis according to two or more studies (OR 1.29 [95% CI 1.10–1.52], $P<0.01$; $n=15$ (11%), $P=0.04$) [21, 23]. Table 3 presents all perioperative and postoperative characteristics that were studied as potential risk factors. A prolonged duration of the resection was a significant risk factor in two studies (OR 18.7 [95% CI 3.07–114], $P<0.01$; OR 1.55 [95% CI 1.04–2.30], $P=0.03$) [22, 23]. Furthermore, benign disease was significantly associated with postoperative cholangitis in two studies (OR 18.5 [95% CI 3.56–100], $P<0.01$; OR 5.3 [95% CI 1.8–15.8]) [22, 25]. Complementary to this, patients with malignant disease were less likely to develop postoperative cholangitis in one study (OR 0.3 [95% CI 0.11–0.39], $P=0.04$) [23]. Postoperative pancreatic fistula was significantly associated with postoperative cholangitis in three studies (OR 2.32 [95% CI 1.29–4.18], $P<0.01$; $n=9$ (8%), $P<0.01$; $n=4$ (3%), $P=0.04$) [19, 22, 24]. Postoperative serum alkaline phosphatase was found to be a significant risk factor in two studies (OR 3.81 [95% CI 1.52–9.55], $P<0.01$; OR 6.03 [95% CI 1.36–6.81], $P=0.02$) [21, 22].

Discussion

This systematic review shows great variation with regard to baseline and perioperative risk factors for postoperative cholangitis after pancreatoduodenectomy in the current literature. Several risk factors that were identified in some studies, were not confirmed by others. Factors that were found to be significantly associated with postoperative cholangitis in two or more studies were a high preoperative BMI, a longer duration of surgery, benign disease, postoperative pancreatic fistula, and increased serum postoperative alkaline phosphatase.

Even though there has been a decrease in mortality resulting from biliary complications after pancreatoduodenectomy, an increase in costs and length of hospital stay in these patients is observed [27]. A previous study demonstrated that almost 25% of the patients with postoperative cholangitis experienced more than ten episodes [22]. Since cholangitis can rapidly progress to sepsis, potentially leading to organ failure and death, it remains crucial to improve our understanding of this complication [22]. Furthermore, the relatively frequent occurrence of postoperative cholangitis without an identifiable cause and lack of a true definition make the diagnosis difficult [26]. Knowledge on risk factors of this complication may help us understand the pathophysiology and how to treat it properly. This systematic review illustrates, however, that it remains difficult to determine which of the studied characteristics should be considered a risk factor for development of postoperative cholangitis.

Complementary to our results, previous studies on postoperative cholangitis in other study populations show conflicting findings as well. One previous systematic review was performed that focused on the incidence and risk factors for cholangitis following biliary-enteric anastomosis in general [4]. Subgroup analysis showed male sex to be a significant risk factor [4]. This is in contrast to our review, where gender was not a significant risk factor. In accordance to our study, preoperative biliary drainage, diabetes, and perioperative blood transfusion were not significantly associated with the development of postoperative cholangitis [4]. Postoperative pancreatic fistula was also not associated with postoperative cholangitis, which, conversely, was a risk factor in three studies included in the current review [4]. Furthermore, the previous systematic review also identified age as a risk factor, which was only confirmed by one out of eight studies included in our study [4]. Nevertheless, both systematic reviews demonstrated the inconsistencies with regard to risk factors for postoperative cholangitis after either pancreatoduodenectomy, or biliary-enteric anastomosis in general.

There are several potential explanations for the conflicting results between studies presented in this systematic review. First, as previously mentioned, multiple studies assessed a combination of cholangitis with biliary stricture or stenosis of the hepaticojejunostomy. This does not only affect the number of patients in the postoperative cholangitis group, but also affects the characteristics of the group and risk factors for cholangitis. In this way, the potential selection bias increases. Furthermore, different definitions of postoperative cholangitis were used in the included studies. Even though four studies used the Tokyo Guidelines to define cholangitis, four others used different definitions. One study did not describe a clear definition [19]. Additionally, classification of potential risk factors partially differed between the included studies (e.g., volume blood loss and duration of surgery).

There is limited evidence for the pathophysiological mechanisms of the potential risk factors presented in this review. Obesity has been associated with a higher frequency of postoperative morbidity in general [28]. An increased risk of postoperative cholangitis in these patients may be due to the reduced manoeuvrability of the intestinal loop, complicating the reconstruction of the hepaticojejunostomy. In the same way, an extended duration of the surgical procedure could be the result of surgical difficulties (e.g., small bile duct) which may increase the risk of developing biliary strictures or stenosis of the hepaticojejunostomy [29]. Moreover, an increased overall survival in patients with benign disease might explain their increased risk for postoperative

Table 2 Patient characteristics

Author (year)		Brown and Zenati [18]	Brown and Jung [19]	Ito [20]	Ueda [21]	Asano [22]	Hiyoshi [23]	Malgras [24]	Parra-membrives [25]
Sample size, n		628	241	133	113	213	161	352	86
Postoperative cholangitis, *n* (%)		50 (8)	27 (11)	28 (21)	21 (19)	16 (8)	13 (8)	20 (6)	14 (16)
Predictive patient characteristics									
Age	*n* (%)	N/A	N/A	11 (8)	10 (9)	N/A	N/A	N/A	N/A
	mean ± SD		66.0 ± 8.3	N/A	N/A		66.5 ± 13.1		
	P-value		0.69	0.67	**0.044**		0.36		
	OR (95% CI)	1.24 (0.77–1.99)[a]	1.60 (0.74–3.50)	N/A	N/A	1.09 (0.67–1.77)	N/A		
	P-value	0.38	0.24			0.725			
Sex	*n* (%)	N/A	9 (4)	17 (13)	17 (15)	N/A	11 (7)	N/A	10 (12)
	mean ± SD		N/A	N/A	N/A		N/A		N/A
	P-value		0.21	0.73	0.39		0.06		0.080
	OR (95% CI)	1.34 (0.83–2.16)	N/A	N/A	N/A	0.33 (0.9–1.19)	N/A		N/A
	P-value	0.24				0.090			
BMI	*n* (%)	N/A	N/A	15 (11)	2 (2)	N/A	N/A	N/A	N/A
	mean ± SD		28.1 ± 5.3	N/A	N/A				
	P-value		0.58	**0.039**	0.23				
	OR (95% CI)	1.55 (0.95–2.54)	1.58 (0.71–3.56)	2.15 (0.89–5.17)	N/A	1.29 (1.10–1.52)			
	P-value	0.081	0.26	0.089		**0.002**			
DM	*n* (%)	N/A	N/A	N/A	5 (4)	N/A	3 (2)	N/A	N/A
	mean ± SD				N/A		N/A		
	P-value				0.55		0.80		
	OR (95% CI)				N/A	1.03 (0.32–3.35)	N/A		
	P-value					0.961			
CCI	*n* (%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD		2.4 ± 1.1						
	P-value		0.44						
	OR (95% CI)	0.88 (0.73–1.07)	N/A						
	P-value	0.19	N/A						
Prior surgery	*n* (%)	N/A	12 (5)	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD								
	P-value		0.24						
	OR (95% CI)	1.22 (0.76–1.98)	N/A						
	P-value	0.41							
Obstructive jaundice	*n* (%)	N/A	N/A	16 (12)	4 (4)	N/A	N/A	N/A	N/A
	mean ± SD			N/A	N/A				
	P-value			0.86	**0.006**				
	OR (95% CI)			N/A	N/A				
	P-value								

Table 2 (continued)

Author (year)		Brown and Zenati [18]	Brown and Jung [19]	Ito [20]	Ueda [21]	Asano [22]	Hiyoshi [23]	Malgras [24]	Parra-membrives [25]
Preoperative biliary drainage	*n* (%)	N/A	N/A	16 (12)	4 (4)	N/A	9 (6)	N/A	N/A
	mean ± SD			N/A	N/A		N/A		N/A
	P-value			0.097	**0.02**		0.71		0.61
	OR (95% CI)			N/A	N/A		N/A		N/A
	P-value								
Preoperative stent	*n* (%)	N/A	10 (4)	N/A	N/A	N/A	N/A	20 (6)	N/A
	mean ± SD		N/A					N/A	
	P-value		0.12					0.39	
	OR (95% CI)		0.53 (0.23–1.19)			10.32[b] (1.33–79.81)		N/A	
	P-value		0.12			**0.025**			
Preoperative cholangitis	*n* (%)	N/A	N/A	N/A	2 (2)	N/A	1 (1)	11 (3)	N/A
	mean ± SD				N/A		N/A	N/A	
	P-value				0.20		0.71	**0.001**	
	OR (95% CI)				N/A		N/A	N/A	
	P-value								
Preoperative chemotherapy	*n* (%)	N/A	13 (5)	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD		N/A						
	P-value		0.35						
	OR (95% CI)	0.60 (0.34–1.04)	N/A					9.0 (2.3–35.5)	
	P-value	0.069						**0.03**	

Statistically significant results are displayed in bold

BMI body mass index, *DM* diabetes Mellitus, *CCI* Charlson Comorbidity Index, *OR* odds ratio

[a]Age < 65 years

[b]Absence of preoperative stenting

[c]Median (range)

cholangitis. This is supported by the median time to postoperative cholangitis onset, which was 275 (range 30–3 037) days in one study and 7 months (range 2–23) in another [21, 22]. Furthermore, postoperative pancreatic fistula not only causes local inflammation, but also increases the length of hospital stay and the use of antibiotics [30]. This may cause dysbiosis of the gut microbiota, which could play a role in the onset of ascending cholangitis. Interestingly, even though bile duct stenosis is known to be a cause of postoperative cholangitis, a small common bile duct diameter was only a significant risk factor in one out of four included studies [4, 20, 22, 24, 25]. Lastly, higher serum levels of alkaline phosphatase can be signs of impaired bile flow, which allows for colonization of bacteria, causing ascending cholangitis.

One of the main limitations of this systematic review is the use of different definitions of postoperative cholangitis in the included studies. Additionally, the included studies had disparate main outcomes and presented the results differently. We were therefore not able to pool the results appropriately and thoughtfully desisted from performing a meta-analysis. It is difficult to establish which risk factors are truly associated with postoperative cholangitis without a meta-analysis. Hence, we can only demonstrate which characteristics seem to be potential risk factors for postoperative cholangitis.

Further research to risk factors for postoperative cholangitis after pancreatoduodenectomy is recommended. This should include a prospective cohort study with more detailed information on patient characteristics, and peri- and postoperative outcomes. Also, it is crucial for future studies to use a consensus definition for postoperative cholangitis after pancreatoduodenectomy. Ideally, this definition should be standardized and endorsed by consensus meetings or surveys. Since few of the possible risk factors identified in the present systematic review are amenable to intervention, for now they should be used for the design of future studies and

Table 3 Peri- and postoperative characteristics

Author (year)		Brown and Zenati [18]	Brown and Jung [19]	Ito [20]	Ueda [21]	Asano [22]	Hiyoshi [23]	Malgras [24]	Parra-Membrives [25]
Sample size, *n*		628	241	133	113	213	161	352	86
Postoperative cholangitis, *n* (%)		50 (8)	27 (11)	28 (21)	21 (19)	16 (8)	13 (8)	20 (6)	14 (16)
Predictive peri- and postoperative characteristics									
Operation type[a]	*n* (%)	N/A	2 (1)	19 (14)	N/A	N/A	N/A	N/A	N/A
	mean ± SD								
	P-value		0.344	0.10					
	OR (95% CI)	2.24 (1.32–3.81)	N/A	N/A					
	P-value	**0.003**							
Operation time	*n* (%)	N/A	N/A	16 (12)	17 (15)	N/A	N/A	N/A	N/A
	mean ± SD		398.0 ± 64.0	N/A	N/A		636.5 ± 91.4		N/A
	P-value		0.05	0.72	< 0.001		0.21		0.395
	OR (95% CI)		1.01 (1.00–1.01)	N/A	18.7 (3.07–114)	1.55 (1.04–2.30)	N/A		N/A
	P-value		0.052		**0.002**	**0.031**			
Blood loss	*n* (%)	N/A	6 (3)	16 (12)	15 (13)	N/A	N/A	N/A	N/A
	mean ± SD		N/A	N/A	N/A		1743.1 ± 546.6		N/A
	P-value		0.42	0.79	0.062		0.98		0.447
	OR (95% CI)		N/A	N/A	N/A	1.00 (0.99–1.00)	N/A		N/A
	P-value					0.051			
Perioperative radiotherapy	*n* (%)	N/A	2 (1)	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD		N/A						
	P-value		0.11						
	OR (95% CI)	1.84 (0.77–4.36)	9.00 (1.18–68.49)						
	P-value	0.17	**0.034**						
Malignant/benign	*n* (%)	N/A	N/A	27 (20)	14 (12)	N/A	N/A	N/A	N/A
	mean ± SD			N/A	N/A				
	P-value			0.68	**< 0.001**				
	OR (95% CI)			N/A	18.5 (3.56–100)	0.32 (0.11–0.39)		5.3 (1.8–15.8)	
	P-value				**0.001**	**0.035**		**0.001**	
Clavien–Dindo ≥ 3 (C-D)	*n* (%)	N/A	10 (4)	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD		N/A						
	P-value		0.072	N/A	N/A	N/A	N/A	N/A	N/A
	OR (95% CI)	1.56 (0.92–2.62)	N/A						
	P-value	0.097							
Small bile duct diameter	*n* (%)	N/A	N/A	N/A	13 (12)	N/A	N/A	N/A	N/A
	mean ± SD		6.6 ± 2.0		N/A		7.2 ± 2.1		
	P-value		**0.005**		0.087		0.050		
	OR (95% CI)		11.57 (1.54–86.94)		N/A		N/A	0.3 (0.1–1.2)	
	P-value		**0.017**					0.09	
Wound infection	*n* (%)	N/A	N/A	5 (4)	N/A	N/A	N/A	N/A	N/A
	mean ± SD			N/A					
	P-value			0.83					
	OR (95% CI)	1.00 (0.55–1.82)		N/A					
	P-value	0.99							

Table 3 (continued)

Author (year)		Brown and Zenati [18]	Brown and Jung [19]	Ito [20]	Ueda [21]	Asano [22]	Hiyoshi [23]	Malgras [24]	Parra-Membrives [25]
Length of stay	*n* (%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD	N/A	7 (5–9)[b]						
	P-value		0.36						
	OR (95% CI)	1.00 (0.96–1.03)	N/A						
	P-value	0.827							
Readmission < 90 days	*n* (%)	N/A	16 (7)	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD		N/A						
	P-value		**0.034**						
	OR (95% CI)	2.30 (1.42–3.72)	N/A						
	P-value	**0.001**							
Adjuvant therapy	*n* (%)	N/A	12 (5)	N/A	N/A	N/A	N/A	N/A	N/A
	mean ± SD		N/A						
	P-value		0.23						
	OR (95% CI)	0.71 (0.44–1.15)	N/A			0.54 (0.18–1.62)			
	P-value	0.17				0.27			
Postoperative pancreatic fistula	*n* (%)	N/A	1 (0.4)	6 (5)	9 (8)	N/A	4 (3)	N/A	N/A
	mean ± SD		N/A	N/A	N/A		N/A		
	P-value		0.71	0.22	**0.008**		**0.036**		
	OR (95% CI)	2.32 (1.29–4.18)	N/A	N/A	N/A	N/A	N/A		
	P-value	**0.005**							
Pneumobilia	*n* (%)	N/A	N/A	15 (11)	19 (17)	N/A	N/A	N/A	N/A
	mean ± SD			N/A	N/A				
	P-value			0.17	**0.012**				
	OR (95% CI)			N/A	28.8 (2.32–358)				
	P-value				**0.009**				
Delayed gastric emptying	*n* (%)	N/A	N/A	0	5 (4)	N/A	N/A	N/A	N/A
	mean ± SD			N/A	N/A				
	P-value			0.20	0.22				
	OR (95% CI)			N/A	N/A				
	P-value								
Postoperative alkaline phosphatase	*n* (%)	N/A	N/A	20 (15)	15 (13)	N/A	N/A	N/A	N/A
	mean ± SD			N/A	N/A				
	P-value			**0.003**	**0.003**				
	OR (95% CI)			3.81 (1.52–9.55)	6.03 (1.36–6.81)				
	P-value			**0.004**	**0.018**				

Statistically significant results are displayed in bold

[a]Pylorus preserving pancreatoduodenectomy vs pylorus resecting pancreatoduodenectomy

[b]Median (range)

create awareness of the complex problem of postoperative cholangitis. Additionally, a more standardized analysis of patients suspected of postoperative cholangitis could be of value to gain further insight into the pathophysiology.

In conclusion, this systematic review identified multiple potential risk factors for postoperative cholangitis after pancreatoduodenectomy. However, consensus on the definition of postoperative cholangitis is required for future prospective research to determine the true relevance of these risk factors.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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