



## Review

# A systematic review on the incidence and risk factors of surgical site infections following hepatopancreatobiliary (HPB) surgery

Lucy E. Chambers<sup>1</sup>, Aali J. Sheen<sup>2</sup> and Kathryn A. Whitehead<sup>1,\*</sup>

<sup>1</sup> Microbiology at Interfaces, Faculty of Science and Engineering, Manchester Metropolitan University, Manchester M1 5GD, UK

<sup>2</sup> Department of Surgery, Central Manchester NHS Foundation Trust, Oxford Road, Manchester, UK

\* **Correspondence:** Email: [K.A.Whitehead@mmu.ac.uk](mailto:K.A.Whitehead@mmu.ac.uk); Tel: +4401612471157.

**Abstract:** Background: Surgical site infections (SSI) are one of the most common hospital acquired infections and result in increased morbidity, mortality and financial burden on health services. The incidence of SSIs are not clearly defined and infection rates as varied as 20%–40% have been reported. The aim of this study was to systematically review the incidence and risk factors of SSI following HPB surgery. Methods: The database of Medline (via PubMed) was systematically searched from 2013–2022. Articles were screened using the PRISMA statement and those that met the inclusion criteria were included in the study. Results: Sixteen studies were eligible for inclusion in this systematic review. The average incidence of SSI was 29.8%. Key risk factors identified included male gender, open surgery, preoperative biliary stenting and obesity. Conclusions: The incidence of SSI following HPB surgery varied, but it is generally high. A variety of pre-disposing patient factors can affect infection rates following HPB surgery. The results from this study suggest that perhaps laparoscopic surgery should be used where possible, and that there should be an awareness that gender, obesity and the use of stents may increase the incidence of SSIs following these operations.

**Keywords:** surgical site infection; hospital acquired infection; surgery; hepatopancreatobiliary; incidence; risk factor

---

## 1. Introduction

Surgical site infections (SSIs) are the most common type of hospital acquired infections (HAI) [1]. The centre for disease control and prevention (CDC) defines a surgical site

infection (SSI) as an infection that occurs after surgery in the part of the body where the surgery took place [2]. SSIs are divided into three categories: 1) superficial incisional SSIs that infect the skin and subcutaneous tissue; 2) deep incisional SSIs that affect the deep soft tissue; and 3) organ/space SSIs where the infection involves any other part of the anatomy including organs and excluding the incision [3]. It has been suggested up to 60% of SSIs are preventable, [4] yet incidences of SSIs can be as high as 20%–40%, depending on the procedure and methods of data collection [5]. SSIs also increase mortality rates, and it has been suggested that patients with an SSI are 2–11 times more at risk of death compared to patients without a SSI [6]. Approximately 16% of patients that receive HPB surgery are thought to be re-admitted [7] with pancreaticoduodenectomy having the highest re-admission rates of all surgery (15%–20%) [8]. Furthermore, the incidence of SSIs after hepatectomy has been reported to be as high as 20%–40% [5]. Alongside the deleterious physiological and psychological issues of patient infection, SSIs increase the length of hospital stay, [9] which results in an increased financial burden, when considering the extended costs of bed stay (length of stay, LOS), treatment, nursing care and further diagnostics that are required [10]. In addition, when antimicrobial resistant organisms cause SSIs, this can result in a higher financial burden and prolonged hospital stay since they are more difficult to treat [9]. The aim of this work was to determine if there was an association between incidence and risk factors of SSI following HPB surgery.

## 2. Materials and methods

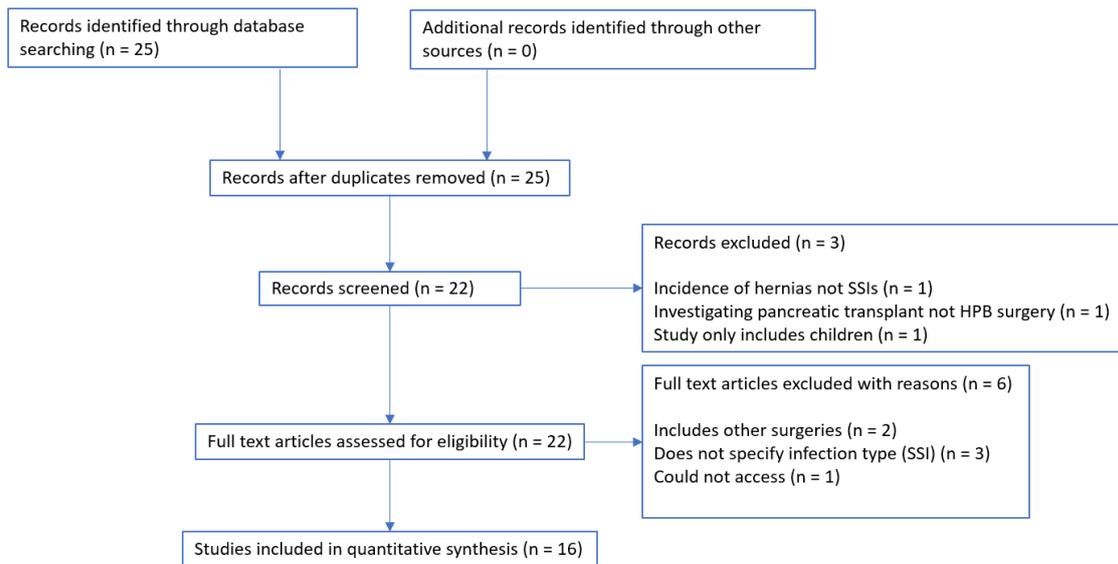
Medline (via PubMed) was searched using the term “(HPB) OR (pancreatic surgery) OR (liver resection) OR (pancreaticoduodenectomy) OR (pancreatectomy) OR (cholecystectomy) AND (surgical site infection) AND (incidence)”. Only studies between 2013–2022 were included and only observational studies including adults. Transplant studies were also excluded. The search was conducted within the Preferred Reporting Items for Meta-Analyses (PRISMA) guidelines [11].

Data on methods, country, surgery type, samples size, total SSI incidence, laparoscopic surgery, SSI definition, type of SSI (superficial, deep, organ and space), the three most frequent bacteria causing SSIs and significant reported risk factors were recorded.

Where enough data was available to determine risk factors of SSIs, odds ratios (95% CI) were calculated, and forest plots were made. These factors were gender, age, weight, open surgery, smoking status, diabetes and use of preoperative biliary drains.

## 3. Results

The initial search resulted in 25 research papers [12–36]. After screening the titles and abstract three articles were excluded (Figure 1) [15,19,29]. These papers were excluded because one looked at the incidence of hernias following HPB surgery and not wound infection, one only focused on pancreatic transplant surgery and one because all of the participants were children. The full texts were then analysed, and six further research papers were excluded [16,17,22,32,35,36]. Two included other surgeries and incidence data on SSI incidence after HPB surgery could not be extracted. Three articles were excluded as they did not specify the type of infection, so SSI incidence could not be distinguished from other postoperative infections. One research paper could not be accessed and thus was not included. A total of 16 papers were then eligible for use in this systematic review.



**Figure 1.** PRISMA eligibility flowchart.

### 3.1. Incidence

The incidence of SSI in the 16 studies varied from 2.0%–54.7% (Table 1). The average incidence of SSI was 29.8%.

### 3.2. Odds ratio for risk factors of SSIs following HPB surgery

#### 3.2.1. Gender

Odds ratio of male gender as a risk factor for SSI was available in 8 studies. Three research papers found male gender to be a significant risk factor of SSI following HPB surgery. Liu et al., 2019 [18] OR 1.17 (95% CI: 1.03, 1.33), Laviano et al., 2020 [12] OR 2.21 (95% CI: 1.25, 2.6) and Algado-Sellés et al., 2022 [14] OR 1.54 (95% CI: 1.05, 2.26) (Figure 2).

**Table 1.** Methods, country, sample size, SSI incidence and surgical factors of the 16 studies. NR = Not recorded.

First author, year	Methods	Country	Surgery type(s)	Sample size	Total SSI	Laparoscopic	SSI definition	Superficial	Deep SSI	Superficial and organ space	Organ space SSI
Laviano et al., 2020 [12]	Observational, prospective	Spain	Cholecystectomy, pancreaticoduodenectomy, total pancreatectomy, segmentectomy, hepatectomy, hepaticojejunostomy and exploratory laparotomy	321	25.80%	35%	NR	4%	4%		92%
Joliat et al., 2018 [13]	Observational, retrospective	Switzerland	Pancreatic	529	26%	NR	CDC	48.60%	NR	34.70%	16.70%
Algado-Sellés et al., 2022 [14]	Observational, prospective, cohort	Spain	Cholecystectomy	2,200	5%	88.70%	CDC	NR	NR	NR	NR
Bortolotti et al., 2021 [17]	Observational, retrospective, monocentric	France	Pancreaticoduodenectomy	129	14.80%	0%	CDC				100%

*Continued on next page*

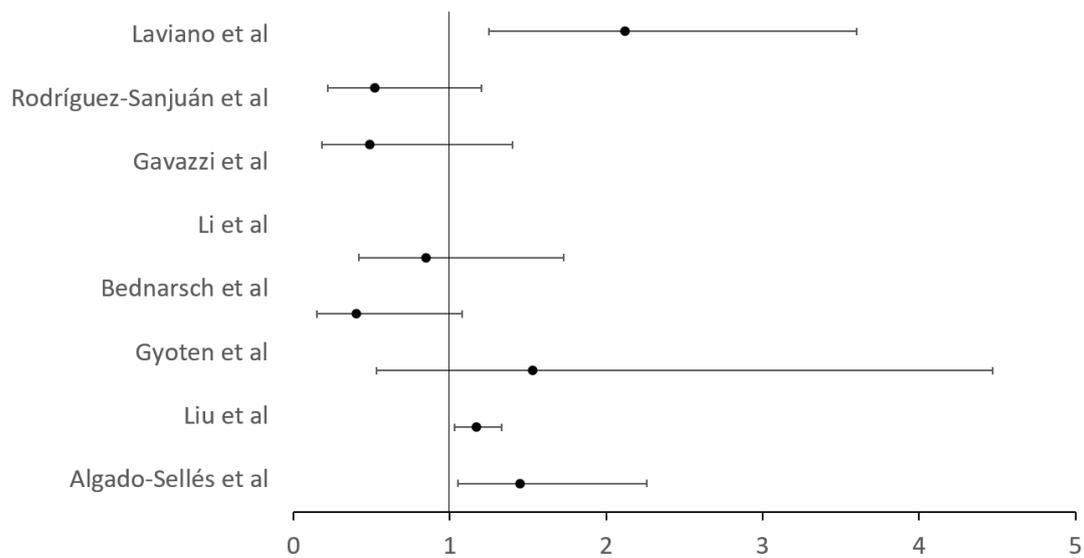
First author, year	Methods	Country	Surgery type(s)	Sample size	Total SSI	Laparoscopic	SSI definition	Superficial	Deep SSI	Superficial and organ space	Organ space SSI
Liu et al., 2019 [18]	Observational, cohort	USA	Pancreatoduodenectomy	5969	20.30%	0%	CDC	7.20%			14.10%
Sert et al., 2022 [20]	Observational	Turkey	Pancreaticoduodenectomy	45	40%	0%	NR	NR	NR	NR	NR
Gyoten et al., 2021 [21]	Observational, prospective	Japan	Pancreaticoduodenectomy, distal pancreatectomy for pancreatic ductal adenocarcinoma (PDAC), total pancreatectomy, major hepatectomy of three segments or more, anatomical sectionectomy and subsectionectomy, common bile duct resection for congenital biliary disease, and liver transplantation	66	30.30%	0%	CDC	NR	NR	NR	NR
Bednarsch et al., 2021 [23]	Observational, cohort	Germany	Liver resection with mandatory portal vein reconstruction (and hepatoduodenopancreatectomy on demand)	95	54.70%	0%	Postoperative abdominal infection	NR	NR	NR	NR

*Continued on next page*

First author, year	Methods	Country	Surgery type(s)	Sample size	Total SSI	Laparoscopic	SSI definition	Superficial	Deep SSI	Superficial and organ space	Organ space SSI
Wagle et al., 2020 [24]	Retrospective, observational	India	Hepatectomy	19	36.80%	0%	CDC	NR	NR	NR	NR
Herzog et al., 2015 [25]	Retrospective, observational, cohort	Germany	Pancreatic head resection or palliative bypass procedures	887	10%	NR	CDC	NR	NR	NR	NR
Li et al., 2017 [26]	Observational, retrospective	China	Hepatectomy combined with hepaticojejunostomy	335	10.15%	0%	CDC	0	0	0	100%
Bhayani et al., 2014 [27]	Observational, retrospective	USA	Pancreaticoduodenectomy, total pancreatectomy	6512	19.30%	0%	NR	NR	NR	NR	NR
Gavazzi et al., 2016 [28]	Observational, retrospective	Italy	Pancreaticoduodenectomy	178	20.80%	NR	CDC	11.80%	9%		26.80%
Rodríguez-Caravaca et al., 2016 [30]	Observational, retrospective	Spain	Cholecystectomy	766	1.96%	77%	NR	0.91%	0.52%		0.52%

*Continued on next page*

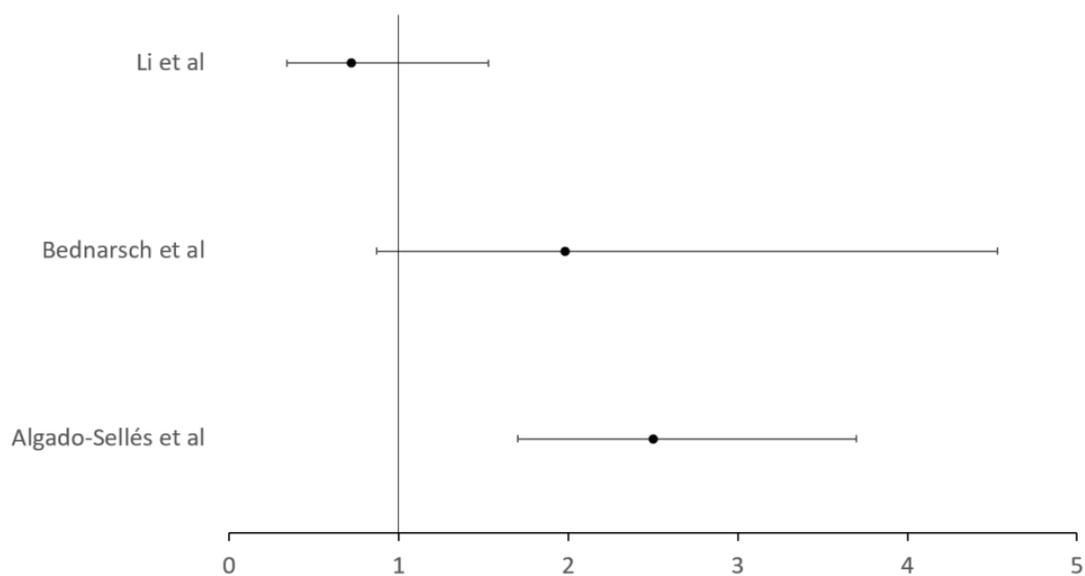
First author, year	Methods	Country	Surgery type(s)	Sample size	Total SSI	Laparoscopic	SSI definition	Superficial	Deep SSI	Superficial and organ space	Organ space SSI
Rodríguez-Sanjuán et al., 2013 [31]	Observational, prospective	Spain	Cholecystectomy	287	8.40%	73.90%	CDC	5.20%			3.10%
Comajuncosas et al., 2014 [33]	Observational, prospective	Spain	Cholecystectomy	220	17.70%	100%	CDC	NR	NR	NR	NR
De Pastena et al., 2018 [34]	Observational, retrospective	Italy	Pancreaticoduodenectomy	387	18%	NR	Clavien–Dindo classification	NR	NR	NR	NR
Huang et al., 2015 [36]	Observational, retrospective	China	Pancreaticoduodenectomy	270	35.60%	NR	Clavien–Dindo classification	16.60%	NR	NR	18.90%



**Figure 2.** Forest plot of odds ratio of male gender and SSI (95% CI).

### 3.2.2. Age

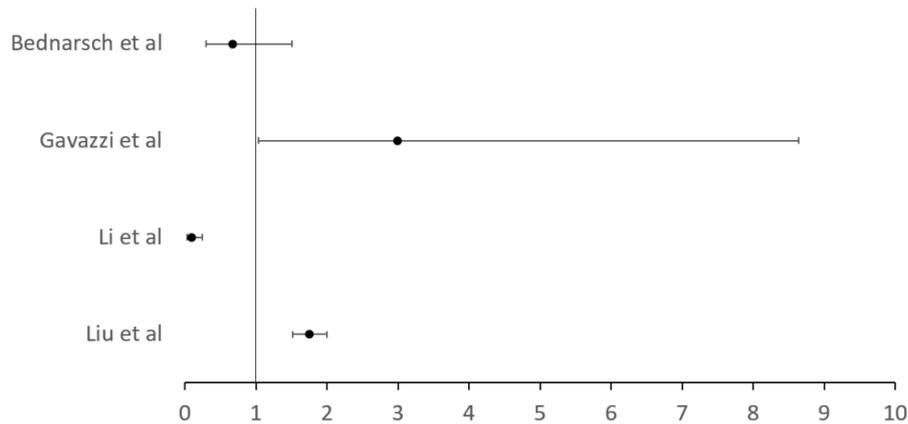
Three studies were suitable for the determination of odds ratio of an age of >65. Of these, only Algado-Sellés et al., 2022 [14] found older age to be a significant risk factor of SSIs (OR 2.5 95% CI: 1.7, 3.7) (Figure 3).



**Figure 3.** Forest plot of odds ratio of age >65 and SSI (95% CI).

### 3.2.3. Obesity

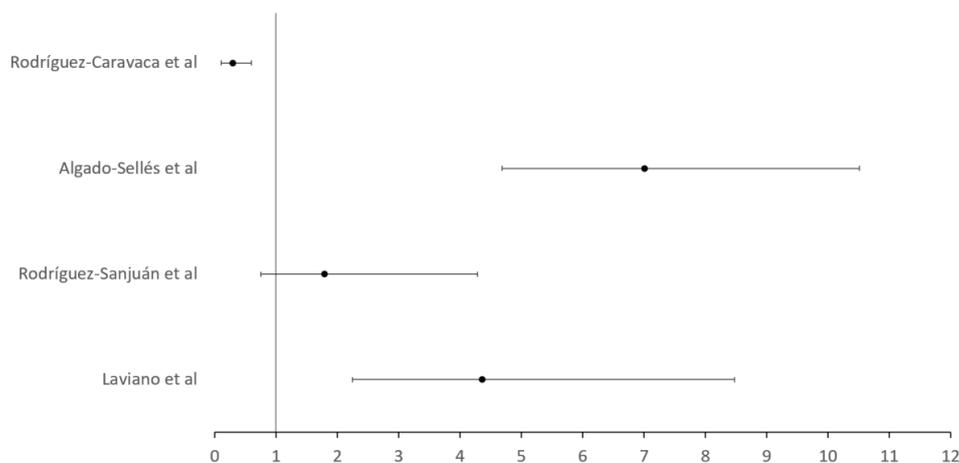
Although other articles than the four used, contained details of weight, a BMI >25 was the only measurement of weight used that was identical in multiple studies. A BMI of over 25 includes obese and overweight patients. Two of the four studies analysed found BMI >25 to be a significant risk factor (Figure 4). Gavazzi et al., 2016 [28] OR 2.99 (95% CI: 1.03, 8.64) and Liu et al., 2019 [18] OR 1.75 (95% CI: 1.52, 2.0). Rodríguez-Caravaca et al., 2016 [30] also found obesity to be a risk factor.



**Figure 4.** Forest plot of odds ratio of BMI >25 and SSI (95% CI).

### 3.2.4. Open surgery

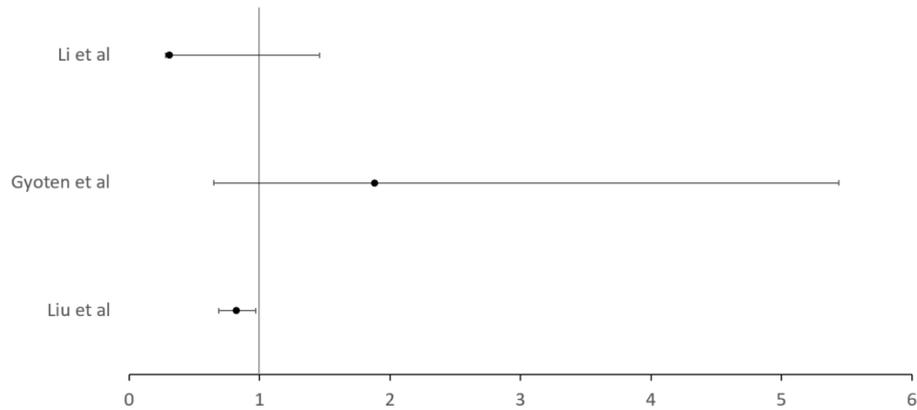
Eight of the 16 studies did not include any laparoscopic procedures. Four research articles had the required data to do an odds ratio analysis. Of these, Algado-Sellés et al., 2022 [14] (OR 7.01 (95% CI: 4.68, 10.51)) and Laviano et al., 2020 [12] (OR 4.36 (95% CI: 2.25, 8.47)) found open surgery to be a significant risk factor of SSIs following HPB surgery (Figure 5).



**Figure 5.** Forest plot of odds ratio of open surgery and SSI (95% CI).

### 3.2.5. Smoking status

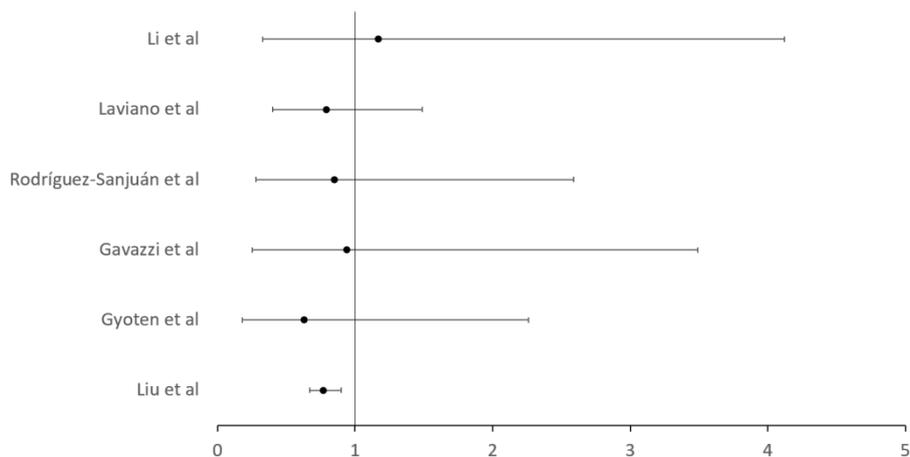
Of the three eligible studies for calculating odds ratio of smoking as a risk factor for SSI, none showed this as a significant risk factor (Figure 6). Furthermore, none of the 18 articles in this review reported smoking as significant risk factor for SSI following HPB surgery.



**Figure 6.** Forest plot of odds ratio of smoking status and SSI (95% CI).

### 3.2.6. Diabetes

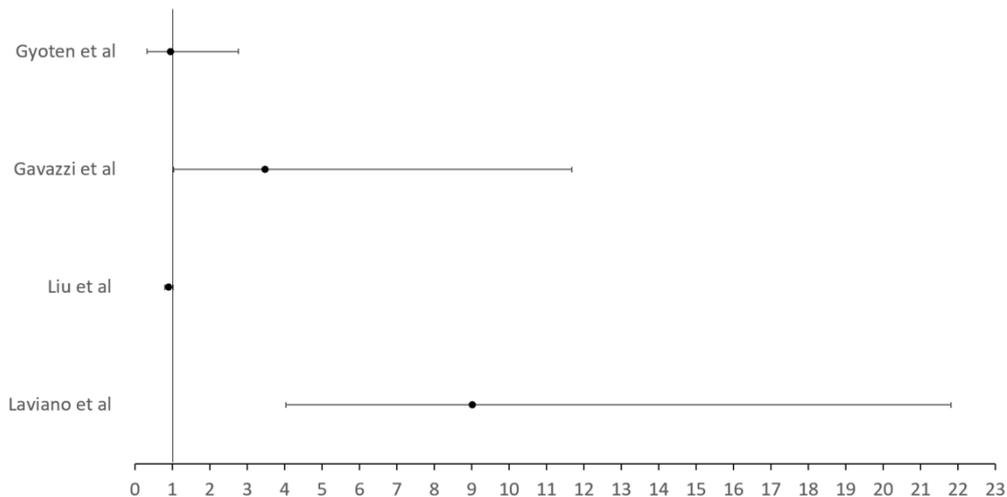
Six research articles were eligible to be included in the odds ratio calculation for diabetes as a risk factor of SSI. Diabetes type 1 and type 2 were differentiated in the studies used. None of these four studies found diabetes to be a significant risk factor of SSIs following HPB surgery (Figure 7). However, Rodríguez-Caravaca et al., 2016 [30] identified diabetes mellitus as an intrinsic risk factor (14.8%).



**Figure 7.** Forest plot of odds ratio of diabetes and SSI (95% CI).

### 3.2.7. Preoperative biliary stent

Four studies were eligible to perform odds ratio analysis on preoperative biliary stenting as a risk factor of SSIs. Of these, only Laviano et al., 2020 [12] found preoperative biliary stenting to be a significant risk factor of SSI (OR 9.01, 95% CI: 4.04, 21.8) (Figure 8).



**Figure 8.** Forest plot of odds ratio of preoperative biliary stent and SSI (95% CI).

### 3.2.8. Microorganisms

*E. coli* and *Enterococcus* spp. were the most frequently identified causes of SSIs (Table 2). One study found that following HPB surgery (hepatectomy with and without biliary tract resection, pancreatectomy [pancreaticoduodenectomy (PD), others], and open cholecystectomy) *Enterococcus* spp. (36%) were the leading cause of SSIs followed by *S. aureus* (14%) (methicillin resistant *Staphylococcus aureus* (MRSA) 8.6%), *Klebsiella* spp. (11%), *Pseudomonas aeruginosa* (8%) and *Enterobacter* spp. (6%) [37]. Both *E. coli* and *Enterococcus* spp. are part of the normal gastrointestinal flora. The fact that these species along with other Enterobacteriaceae species were identified as the cause of SSI might imply that the infection occurred due to contamination from the patient's own gastrointestinal flora.

**Table 2.** The most commonly reported causative organisms of SSIs and the reported risk factors for SSIs in the 16 research papers.

First Author, year	Three most commonly reported organisms of SSIs	Key risk factors of SSIs
Laviano et al., 2020 [12]	Other GN (22.1%), <i>E. coli</i> (18.3%), Other GPs (16.3%)	Male, protein malnutrition, neoplasms, hospitalization in last 18 months, open surgery, transfusions, vasopressors, elective, pancreaticoduodenectomy
Joliat et al., 2018 [13]	NR	Male, biliary stenting, anastomosis
Algado-Sellés et al., 2022 [14]	<i>E. coli</i> (35%), <i>E. faecalis</i> (13.3%), <i>E. faecium</i> (8.3%)	Age, pre-surgical glycemia, laparoscopic technique, time of the intervention, type of surgery and NNIS index.
Bortolotti et al., 2021 [17]	(Bile cultures) <i>E. coli</i> (19%), <i>Klebsiella</i> spp. (14%), <i>Enterococcus</i> spp. (12.47%)	NR
Liu et al., 2019 [18]	NR	Male, non-White, hispanic, obese, small pancreatic duct, longer operation.
Sert et al., 2022 [20]	NR	NR
Gyoten et al., 2021 [21]	<i>E. faecalis</i> , Coagulase negative <i>Staphylococci</i> , <i>Enterobacter</i> spp.	Gastric Candida colonization
Bednarsch et al., 2021 [23]	<i>Enterococcus faecium</i> 71.2%), <i>Enterococcus faecalis</i> (30.8%), <i>Enterobacter cloacae</i> (25%)	Reduced susceptibility to perioperative antibiotic prophylaxis, Portal vein embolization, Other postoperative infections, increased hospital and ICU stay
Wagle et al., 2020 [24]	NR	NR

*Continued on next page*

First Author, year	Three most commonly reported organisms of SSIs	Key risk factors of SSIs
Herzog et al., 2015 [25]	<i>Enterococcus</i> spp. (41%) <i>E. coli</i> (17%) MRSA (12%)	Positive bile duct cultures
Li et al., 2017 [26]	<i>E. coli</i> (25%), <i>S. epidermidis</i> (12.5%), <i>Pseudomonas</i> spp./ <i>Streptococcus</i> spp./MRSA (8.3%)	Coexisting cholangiolithiasis, blood loss >1500mL, previous abdominal surgical history, bile leak
Bhayani et al., 2014 [27]	NR	NR
Gavazzi et al., 2016 [28]	(Drain fluid) <i>Enterococcus</i> spp. (69.1%), <i>E. coli</i> (26.8%), <i>Staphylococcus</i> spp. (26.8%)	BMI $\geq$ 25 kg/m <sup>2</sup> , biliary stenting, cardiac disease
Rodríguez-Caravaca et al., 2016 [30]	<i>E. coli</i> (47.8%), <i>Klebsiella pneumoniae</i> (13.1%). <i>E. faecium</i> (13.1%)	Open surgery, renal failure, diabetes mellitus, malignancy, chronic obstructive pulmonary disease, liver cirrhosis, obesity, neutropenia, neoplasia
Rodríguez-Sanjuán et al., 2013 [31]	<i>E. coli</i> (26.5%), <i>Streptococcus</i> spp. (19.4%), <i>Enterococcus</i> spp. (17.3%)	Open surgery, conversion to open surgery
Comajuncosas et al., 2014 [33]	NR	NR
De Pastena et al., 2018 [34]	(Bile cultures) <i>E. coli</i> (19.9%), <i>E. faecalis</i> (18.8%), <i>Klebsiella</i> spp. (17.7%)	Positive rectal swab, preoperative biliary drain
Huang et al., 2015 [36]	NR	Endoscopic retrograde biliary stent

\*Note: NR = Not recorded; GP = Gram positive; GN = Gram negative

## 4. Discussion

### 4.1. Risk factors

#### 4.1.1. Gender

Male sex was found to be a risk factor of SSI following HPB surgery in three of the eight studies analysed. Indeed, it has been it had been previously demonstrated that men were generally at a higher risk of SSI following various surgeries [38]. A surveillance study in Germany found that SSI rates were significantly higher for male patients who had abdominal surgeries, including cholecystectomies [39], and a prevalence study investigating predictors of colonization with *Staphylococcus* spp. in patients undergoing cardiac and orthopaedic surgery found significantly higher colonization rates in men [40]. However, Enterobacteriaceae are the predominant bacteria that cause SSIs following HPB surgery and hence this area requires further investigation.

#### 4.1.2. Age

One of the three studies included in the analysis found that people of an older age (>65) were more likely to be at a risk factor of SSIs [41,42]. For example, Ansari et al., 2019 found that SSIs were more common in older participants (11.4% vs. 6.4%;  $p = 0.009$ ) [43]. Conversely, others have found that the risk of SSI decreases as age increases, although these studies have small sample sizes [44]. It is difficult to determine if older age results in comorbidities which may be risk factors of SSIs or immunologic senescence as patients age is a risk factor of SSI [45]. Older patients are more likely to have surgery and the population is progressively aging, therefore surgeries and surgical site infection incidence in older patients is likely to increase [46].

#### 4.1.3. Obesity

Three studies found obesity to be a risk factor of SSIs. Due to unhealthy lifestyle habits obesity is becoming more prevalent, particularly in western countries. Obesity is a known risk factor for many types of SSI [5], although many obese patients may also have other comorbidities such as type II diabetes (T2DM), coronary heart disease and osteoarthritis; this makes it difficult to determine if obesity is a single causative risk factor of SSIs. Another factor to consider is that operating times in obese patients are often longer and this is an independent risk factor in the development SSIs. Thelwall et al., 2015 found that in patients undergoing abdominal hysterectomy, knee replacement and large bowel surgery, the risk of SSI increased approximately linearly with increasing BMI [47]. However, HPB surgery was not specifically included in this research and laparoscopic procedures were not included in the cohort due to a recognised lower risk of infection [47].

A study in Shanghai (China) between 2010 and 2011, aimed to identify the risk factors for SSIs following hepatic resection in 7,388 patients and of these participants, 27.3% were obese, and hence the results showed that obesity significantly predicted incisional SSI but no other forms of SSIs [48]. It is thought that high infection rates in obese patients occurs due to tissue oxygen pressure and Kabon et al., (2004) concluded that wound and tissue hypoxia commonly occurred in obese patients perioperatively [49]. SSIs may also occur in obese patients due to reduced blood circulation in the fat tissues which results in a reduced circulation of the immune cells and hence a reduced propensity of the body to eradicate bacteria [50].

#### 4.1.4. Type of surgery

The steady transition from open to minimally invasive surgery (laparoscopic) or keyhole surgery is becoming apparent with more operations now undertaken via laparoscopic techniques. There is evidence to suggest that infections rates are lower in patients following laparoscopic procedures rather than open surgery. Indeed, this meta-analysis found two of the four studies analysed showed open surgery to be risk factors of SSIs. Another meta-analysis found that when laparoscopic abdominal surgery was compared to open surgery, the incidence of SSIs was reduced by 70%–80% following laparoscopic surgery in obese patients [51]. In a case-matched control study of 50 patients, López-Ben et al. (2014) found that the rates of SSIs in laparoscopic surgery patients was 2%, whilst 18% of open surgery patients developed a SSI [52]. However, this study also found that the mean operating time for laparoscopic surgery was 95 minutes longer than for open surgery. Thus, the relationship between the

incidence of an SSI, length of operation time and type of operation carried out needs further investigation, but it appears that a larger wound may have an effect on increasing wound infection rates when considered along with the length of the operation.

Although less frequent SSIs can still occur following laparoscopic surgery these are referred to as port site infections (PSI). Similar species cause SSIs and PSIs although Mir et al., found that *Pseudomonas* spp. (42.2%) was the common offending organism in PSIs following laparoscopic cholecystectomy [53]. The source of these infections was found to be the water used to wash surgical instruments.

#### 4.1.5. Smoking

None of the 16 studies highlighted smoking a risk factor for SSI and hence the three studies included in statistical analysis did not identify smoking as a significant risk factor. In contrast, a number of studies have found that smoking increases the risk of SSIs. A meta-analysis identified a range of cohort studies and randomized controlled trials that found a higher incidence of SSIs in smokers [54]. Nicotine use is known to delay primary wound healing [55] and thus the longer a wound takes to heal, the greater the propensity for it to become infected. Nicotine can cause vasoconstriction resulting in reduces cutaneous blood flow; stimulate the release of proteases that accelerate tissue destruction and suppress the immune response, increasing the risk of bacterial infection [56]. However, another factor to take into account is that smoking is known to cause respiratory and cardiovascular disease and thus it might be these clinical manifestations that increase the risk of developing a SSI and not primarily smoking alone [57]. Furthermore, other factors such as how long an individual has smoked and the amount of cigarettes smoked may influence SSI occurrence.

#### 4.1.6. Diabetes

Diabetes is considered a risk factor for many infectious diseases and infections. Diabetes is becoming more prevalent with the number of people with diabetes more than doubling in the last 20 years in the UK [58]. In the studies included in this review only Rodríguez-Caravaca et al., 2016 [30] found diabetes to be an intrinsic risk factor of SSI following HPB surgery.

There is a large body of evidence suggesting diabetes is a risk factor. Barreto et al., (2015) found that when patients with T2DM underwent surgery, they were at a greater risk of developing a SSI [59]. Indeed, a meta-analysis of 14 studies found that patients with diabetes were almost twice as likely to develop a SSI when compared to non-diabetic patients [60]. A number of reasons can explain the higher rates of SSIs in diabetic patients; firstly, diabetic patients often suffer from small vessel disease where there is a decrease in nutrients and oxygen flow to peripheral tissues and thus reduced systemic ability to fight infections [61]. Secondly, high blood glucose levels impair the function of monocytes and leukocytes, resulting in decreased phagocytosis of bacterial cells [62]. Finally, diabetic patients often experience peripheral neuropathy, and this decreases the release of neuropeptides, disrupting the healing response [63]. Furthermore, T2DM has been found to reduce bacterial diversity of the skin microbiome [64]. The skin microbiome protects against infection due to competitive exclusion and direct inhibition.

#### 4.1.7. Preoperative biliary drains

Preoperative biliary stenting was significantly associated with SSI in two of the four research articles included in this analysis. De Pastena et al., 2018 [34] and Joliat et al., 2018 [13] also recorded preoperative biliary stenting as a risk factor of SSIs. In HPB surgery, drains may also be used to remove bile and pancreatic juice, as these are toxic to surrounding tissues. Results from randomised control trials have shown that in hepatic surgery, the use of drains may increase the risk of infections in some patient undergoing a hepatectomy [65]. A meta-analysis found that prophylactic drains did not reduce the occurrence of bile collection which is interesting since this contradicts the objective of this technique [56]. Furthermore, drains may act as a channel for bacteria to spread to the wound, thus increasing the risk of SSIs [66]. Late removal of surgical drains has also been suggested to increase the risk of infections including wound infections, since it has been demonstrated that retrograde drain infections increased when drain placement was prolonged for more than 4 days postoperatively [67]. An explanation for this is that if a drain left in place for more than 4 days bacteria are able to form a biofilm on the foreign object.

#### 4.1.8. Microorganisms

In the 16 studies included, the frequency of the different bacteria found to be causing SSIs varied although there were similarities in the three most commonly found species causing SSIs. In no particular order, the most commonly identified causative species were *E. coli*, *E. faecalis*, *E. faecium*, CoNS, *Klebsiella* spp., *Enterobacter* spp., MRSA, *Pseudomonas* spp. and *Streptococcus* spp. Other researchers have shown similar findings, for example, Shirata et al., 2017 found that incisional SSIs were caused by MRSA (29%), CoNS (21%), *Enterobacter cloacae* (12.5%), methicillin susceptible *Staphylococcus aureus* (MSSA) (8%), *Klebsiella* spp. (4%) and *Enterococcus faecalis* (4%) [68]. Shirata et al., 2017 also found that organ and space SSIs were caused by CoNS (33%), *Enterococcus faecalis* (14%), MRSA (12%), *Enterococcus faecium* (10%), MSSA (8%), *Enterobacter cloacae* (5%), *Streptococcus* spp., *Bacteroides* spp., *Escherichia coli*, *Klebsiella* spp., *Candida* spp. (3%), *Serratia* spp., *Pseudomonas* spp. and other *Enterococcus* spp. (1%) [68]. Another study found that *Enterococcus* spp. (n = 59) were the leading cause of SSIs following HPB surgery followed by *S. aureus* (n = 23 MSSA, n = 14 MRSA), *Klebsiella* spp. (n = 18), *Pseudomonas aeruginosa* (n = 13) and *Enterobacter* spp. (n = 10) [37]. The prevalence of different bacteria on patients and on hospital wards may vary between geographical locations, although gastrointestinal and skin commensals may be the most likely cause of SSIs following HPB surgery.

#### 4.2. Limitations and future work

Eleven of the 16 studies presented in this review were conducted in Europe with five of these being Spain. This could mean that the results are not representative of the SSI incidence in the world due to a location bias. As the studies included were initially screened for incidence results and not risk factors a further metanalysis searching for each separate risk factor would be useful in adding to this body of research.

## 5. Conclusions

A variety of pre-disposing patient factors can affect infection rates following HPB surgery. Pre, intra and post-surgical factors also influence the occurrence of a SSI following HPB surgery. The results from this study suggest that perhaps there is an association between the use of laparoscopic surgery and infection, and that there should be an awareness that gender, obesity and the use of stents may increase the incidence of SSIs following these surgeries. Further, confounding factors could be responsible for the development of an SSI. This complicated relationship between surgical interventions and SSIs merits further investigation and understanding if the incidences of such infections are to be reduced.

### Author contributions

Lucy E. Chambers was responsible for the acquisition, analysis and interpretation of data for the work. Aali J. Sheen and Kathryn A. Whitehead were responsible for the conception and design of the work. All authors were responsible for the drafting and revision of the data and final approval of the version to be published.

### Conflict of interest

The author declares no conflicts of interest in this paper.

### References

1. Zinn J, Jenkins JB, Harrelson B, et al. (2013) Differences in intraoperative prep solutions: a retrospective chart review. *AORN J* 97: 552–558. <http://dx.doi.org/10.1016/j.aorn.2013.03.006>
2. Centre for disease control and prevention, Healthcare-Associated Infections (HAIs), CDC, 2019. Available from: [https://www.cdc.gov/hai/ssi/faq\\_ssi.html](https://www.cdc.gov/hai/ssi/faq_ssi.html).
3. Mangram AJ, Horan TC, Pearson ML, et al. (1999) Guideline for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol* 20: 247–280. <https://doi.org/10.1086/501620>
4. Anderson DJ, Podgorny K, Berríos-Torres SI, et al. (2014) Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 35: 605–627. <https://doi.org/10.1086/676022>
5. Ceppa EP, Pitt HA, House MG, et al. (2013) Reducing surgical site infections in hepatopancreatobiliary surgery. *HPB (Oxford)* 15: 384–391. <https://doi.org/10.1111/j.1477-2574.2012.00604.x>
6. Olson MM and Lee JT (1990) Continuous, 10-year wound infection surveillance: results, advantages, and unanswered questions. *Arch Surg* 125: 794–803. <https://doi.org/10.1001/archsurg.1990.01410180120020>
7. Lucas DJ, Haider A, Haut E, et al. (2013) Assessing readmission after general, vascular, and thoracic surgery using ACS-NSQIP. *Ann Surg* 258: 430–439. <https://doi.org/10.1097/SLA.0b013e3182a18fcc>

8. Martin RC, Brown R, Puffer L, et al. (2011) Readmission rates after abdominal surgery: the role of surgeon, primary caregiver, home health, and subacute rehab. *Ann Surg* 254: 591–597. <https://doi.org/10.1097/sla.0b013e3182300a38>
9. Bassetti M, Merelli M, Temperoni C, et al. (2013) New antibiotics for bad bugs: where are we? *Ann Clin Microbiol Antimicrob* 12: 22. <https://doi.org/10.1186/1476-0711-12-22>
10. Leaper DJ, van Goor H, Reilly J, et al. (2004) Surgical site infection - a European perspective of incidence and economic burden. *Int Wound J* 1: 247–273. <https://doi.org/10.1111/j.1742-4801.2004.00067.x>
11. Moher D, Liberati DA, Tetzlaff J, et al. (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 339: b2535. <https://doi.org/10.1136/bmj.b2535>
12. Laviano E, Sanchez M, González-Nicolás MT, et al. (2020) Surgical site infection in hepatobiliary surgery patients and its relationship with serum vitamin D concentration. *Cir Esp (Engl Ed)* 98: 456–464. <https://doi.org/10.1016/j.ciresp.2020.03.004>
13. Joliat GR, Sauvain MO, Petermann D, et al. (2018) Surgical site infections after pancreatic surgery in the era of enhanced recovery protocols. *Medicine* 97: e11728. <https://doi.org/10.1097/MD.00000000000011728>
14. Algado-Sellés N, Mira-Bernabeu J, Gras-Valentí P, et al. (2022) Estimated costs associated with surgical site infections in patients undergoing cholecystectomy. *Int J Environ Res Public Health* 19: 764. <https://doi.org/10.3390/ijerph19020764>
15. Alhambra-Rodríguez de Guzmán C, Morandeira-Rivas AJ, Herrero-Bogajo ML, et al. (2020) Incidence and risk factors of incisional hernia after single-incision endoscopic surgery. *J Laparoendosc Adv Surg Tech A* 30: 251–255. <https://doi.org/10.1089/lap.2019.0728>
16. Akhter MS, Verma R, Madhukar KP, et al. (2016) Incidence of surgical site infection in postoperative patients at a tertiary care centre in India. *J Wound Care* 25: 214–217. <https://doi.org/10.12968/jowc.2016.25.4.210>
17. Bortolotti P, Delpierre C, Le Guern R, et al. (2021) High incidence of postoperative infections after pancreaticoduodenectomy: A need for perioperative anti-infectious strategies. *Infect Dis Now* 51: 456–463. <https://doi.org/10.1016/j.idnow.2021.01.001>
18. Liu JB, Baker MS, Thompson VM, et al. (2018) Wound protectors mitigate superficial surgical site infections after pancreatoduodenectomy. *HPB (Oxford)* 21: 121–131. <https://doi.org/10.1016/j.hpb.2018.07.006>
19. Ray S, Ansari Z, Kumar D, et al. (2020) Short- and long-term outcome of surgery for chronic pancreatitis in children: a single surgeon experience. *Pediatr Surg Int* 36: 1087–1092. <https://doi.org/10.1007/s00383-020-04691-3>
20. Sert I, Yesilyurt D, Ertekin SC, et al. (2022) Duct-to-mucosa pancreaticojejunostomy with less serosal stitches: A different approach to well-known problem. *J Coll Physicians Surg Pak* 32: 75–80. <https://doi.org/10.29271/jcpsp.2022.01.75>
21. Gyoten K, Kato H, Hayasaki A, et al. (2021) Association between gastric Candida colonization and surgical site infections after high-level hepatobiliary pancreatic surgeries: the results of prospective observational study. *Langenbecks Arch Surg* 406: 109–119. <https://doi.org/10.1007/s00423-020-02006-7>

22. Suenaga M, Yokoyama Y, Fujii T, et al. (2021) Impact of preoperative occult-bacterial translocation on surgical site infection in patients undergoing pancreatoduodenectomy. *J Am Coll Surg* 232: 298–306. <https://doi.org/10.1016/j.jamcollsurg.2020.12.001>
23. Bednarsch J, Czigany Z, Heij LR, et al. (2021) Bacterial bile duct colonization in perihilar cholangiocarcinoma and its clinical significance. *Sci Rep* 11: 2926. <https://doi.org/10.1038/s41598-021-82378-y>
24. Wagle P, Narkhede R, Desai G, et al. (2020) Surgical management of large hepatocellular carcinoma: the first single-center study from western india. *Arq Bras Cir Dig* 33: e1505. <https://doi.org/10.1590/0102-672020190001e1505>
25. Herzog T, Belyaev O, Akkuzu R, et al. (2015) The impact of bile duct cultures on surgical site infections in pancreatic surgery. *Surg Infect (Larchmt)* 16: 443–449. <https://doi.org/10.1089/sur.2014.104>
26. Li L, Ding J, Han J, et al. (2017) A nomogram prediction of postoperative surgical site infections in patients with perihilar cholangiocarcinoma. *Medicine* 96: e7198. <https://doi.org/10.1097/MD.00000000000007198>
27. Bhayani NH, Miller JL, Ortenzi G, et al. (2014) Perioperative outcomes of pancreaticoduodenectomy compared to total pancreatectomy for neoplasia. *J Gastrointest Surg* 18: 549–554. <https://doi.org/10.1007/s11605-013-2393-0>
28. Gavazzi F, Ridolfi C, Capretti G, et al. (2016) Role of preoperative biliary stents, bile contamination and antibiotic prophylaxis in surgical site infections after pancreaticoduodenectomy. *BMC Gastroenterol* 16: 43. <https://doi.org/10.1186/s12876-016-0460-1>
29. Gasteiger S, Cardini B, Göbel G, et al. (2018) Outcomes of pancreas retransplantation in patients with pancreas graft failure. *Br J Surg* 105: 1816–1824. <https://doi.org/10.1002/bjs.10929>
30. Rodríguez-Caravaca G, Gil-Yonte P, Risco-Risco C, et al. (2016) Antibiotic prophylaxis in elective cholecystectomy: Protocol adequacy and related outcomes in a retrospective single-centre analysis. *Rev Esp Enferm Dig* 108: 15–19. <https://doi.org/10.17235/reed.2015.3870/2015>
31. Rodríguez-Sanjuán JC, Casella G, Antolín F, et al. (2013) How long is antibiotic therapy necessary after urgent cholecystectomy for acute cholecystitis? *J Gastrointest Surg* 17: 1947–1952. <https://doi.org/10.1007/s11605-013-2321-3>
32. Olsen MA, Tian F, Wallace AE, et al. (2017) Use of quantile regression to determine the impact on total health care costs of surgical site infections following common ambulatory procedures. *Ann Surg* 265: 331–339. <https://doi.org/10.1097/SLA.0000000000001590>
33. Comajuncosas J, Heroso J, Gris P, et al. (2014) Risk factors for umbilical trocar site incisional hernia in laparoscopic cholecystectomy: a prospective 3-year follow-up study. *Am J Surg* 207: 1–6. <https://doi.org/10.1016/j.amjsurg.2013.05.010>
34. De Pastena M, Paiella S, Azzini AM, et al. (2018) Preoperative surveillance rectal swab is associated with an increased risk of infectious complications in pancreaticoduodenectomy and directs antimicrobial prophylaxis: an antibiotic stewardship strategy? *HPB (Oxford)* 20: 555–562. <https://doi.org/10.1016/j.hpb.2017.12.002>

35. Feng F, Cao X, Liu X, et al. (2019) Two forms of one complication: Late erosive and nonerosive postpancreatectomy hemorrhage following laparoscopic pancreaticoduodenectomy. *Medicine* 98: e16394. <https://doi.org/10.1097/MD.00000000000016394>
36. Huang X, Liang B, Zhao XQ, et al. (2015) The effects of different preoperative biliary drainage methods on complications following pancreaticoduodenectomy. *Medicine* 94: e723. <https://doi.org/10.1097/MD.0000000000000723>
37. Takahashi Y, Takesue Y, Fujiwara M, et al. (2018) Risk factors for surgical site infection after major hepatobiliary and pancreatic surgery. *J Infect Chemother* 24: 739–743. <https://doi.org/10.1016/j.jiac.2018.05.007>
38. Al-Qurayshi Z, Baker SM, Garstka M, et al. (2018) Post-operative infections: Trends in distribution, risk factors, and clinical and economic burdens. *Surg Infect* 19: 717–722. <https://doi.org/10.1089/sur.2018.127>
39. Langelotz C, Mueller-Rau C, Terziyski S, et al. (2014) Gender-specific differences in surgical site infections: an analysis of 438,050 surgical procedures from the German National Nosocomial Infections Surveillance System. *Viszeralmedizin* 30: 114–117. <https://doi.org/10.1159/000362100>
40. Neidhart S, Zaatreh S, Klinder A, et al. (2018) Predictors of colonization with *Staphylococcus* species among patients scheduled for cardiac and orthopedic interventions at tertiary care hospitals in North-Eastern Germany—a prevalence screening study. *Eur J Clin Microbiol Infect Dis* 37: 633–641. <https://doi.org/10.1007/s10096-017-3154-x>
41. Owens CD and Stoessel K (2008) Surgical site infections: epidemiology, microbiology and prevention. *J Hosp Infect* 70: 3–10. [https://doi.org/10.1016/S0195-6701\(08\)60017-1](https://doi.org/10.1016/S0195-6701(08)60017-1)
42. Graf K, Sohr D, Haverich A, et al. (2009) Decrease of deep sternal surgical site infection rates after cardiac surgery by a comprehensive infection control program. *Interact Cardiovasc Thorac Surg* 9: 282–286. <https://doi.org/10.1510/icvts.2009.205286>
43. Ansari S, Hassan M, Barry HD, et al. (2019) Risk factors associated with surgical site infections: A retrospective report from a developing country. *Cureus* 11: e4801. <https://doi.org/10.7759/cureus.4801>
44. Delgado-Rodriguez M, Gomez-Ortega A, Sillero-Arenas M, et al. (2001) Epidemiology of surgical-site infections diagnosed after hospital discharge: a prospective cohort study. *Infect Control Hosp Epidemiol* 22: 24–30. <https://doi.org/10.7759/cureus.480110.1086/501820>
45. Talbot TR and Schaffner W (2005) Relationship between age and the risk of surgical site infection: A contemporary reexamination of a classic risk factor. *J Infect Dis* 191: 1032–1035. <https://doi.org/10.1086/428627>
46. Agodi A, Quattrocchi A, Barchitta M, et al. (2015) Risk of surgical site infection in older patients in a cohort survey: targets for quality improvement in antibiotic prophylaxis. *Int Surg* 100: 473–479. <https://doi.org/10.9738/INTSURG-D-14-00042.1>
47. Thelwall S, Harrington P, Sheridan E, et al. (2015) Impact of obesity on the risk of wound infection following surgery: results from a nationwide prospective multicentre cohort study in England. *Clin Microbiol Infect* 21: 1008.e1–1008.e8. <https://doi.org/10.1016/j.cmi.2015.07.003>
48. Yang T, Tu PA, Zhang H, et al. (2014) Risk factors of surgical site infection after hepatic resection. *Infect Control Hosp Epidemiol* 35: 317–320. <https://doi.org/10.1086/675278>

49. Kabon B, Nagele A, Reddy D, et al. (2004) Obesity decreases perioperative tissue oxygenation. *Anesthesiology* 100: 274–280. <https://doi.org/10.1097/00000542-200402000-00015>
50. Ye J (2011) Adipose tissue vascularization: its role in chronic inflammation. *Curr Diab Rep* 11: 203–210. <https://doi.org/10.1007/s11892-011-0183-1>
51. Shabanzadeh DM and Sørensen LT (2012) Laparoscopic surgery compared with open surgery decreases surgical site infection in obese patients: a systematic review and meta-analysis. *Ann Surg* 256: 934–945. <https://doi.org/10.1097/SLA.0b013e318269a46b>
52. López-Ben S, Palacios O, Codina-Barreras A, et al. (2014) Pure laparoscopic liver resection reduces surgical site infections and hospital stay. Results of a case-matched control study in 50 patients. *Langenbecks Arch Surg* 399: 307–314. <https://doi.org/10.1007/s00423-014-1169-7>
53. Mir MA, Malik UY, Wani H, et al. (2013) Prevalence, pattern, sensitivity and resistance to antibiotics of different bacteria isolated from port site infection in low risk patients after elective laparoscopic cholecystectomy for symptomatic cholelithiasis at tertiary care hospital of Kashmir. *Int Wound J* 10: 110–113. <https://doi.org/10.1111/j.1742-481X.2012.00963.x>
54. Sørensen LT (2012) Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. *Ann Surg* 255: 1069–1079. <https://doi.org/10.1097/SLA.0b013e31824f632d>
55. Shi L, Wu Y, Yang C, et al. (2019) Effect of nicotine on *Staphylococcus aureus* biofilm formation and virulence factors. *Sci Rep* 27: 20243. <https://doi.org/10.1038/s41598-019-56627-0>
56. Rietbrock N, Kunkel S, Wörner W, et al. (1992) Oxygen-dissociation kinetics in the blood of smokers and non-smokers: interaction between oxygen and carbon monoxide at the hemoglobin molecule. *Naunyn Schmiedebergs Arch Pharmacol* 345: 123–128. <https://doi.org/10.1007/BF00175479>
57. Messner B and Bernhard D (2014) Smoking and cardiovascular disease. *Arter Thromb Vasc Biol* 34: 509–515. <https://doi.org/10.1161/ATVBAHA.113.300156>
58. Diabetes UK, Number of people living with diabetes doubles in twenty years, 2018. Available from: [https://www.diabetes.org.uk/about\\_us/news/diabetes-prevalence-statistics#:~:text=The%20number%20of%20people%20diagnosed,of%201.9%20million%20since%201998.](https://www.diabetes.org.uk/about_us/news/diabetes-prevalence-statistics#:~:text=The%20number%20of%20people%20diagnosed,of%201.9%20million%20since%201998.)
59. Barreto SG, Singh MK, Sharma S, et al. (2015) Determinants of surgical site infections following pancreatoduodenectomy. *World J Surg* 39: 2557–2563. <https://doi.org/10.1007/s00268-015-3115-4>
60. Zhang Y, Zheng QJ, Wang S, et al. (2015) Diabetes mellitus is associated with increased risk of surgical site infections: A meta-analysis of prospective cohort studies. *Am J Infect Control* 43: 810–815. <https://doi.org/10.1016/j.ajic.2015.04.003>
61. Turina M, Fry DE, Polk HC Jr (2005) Acute hyperglycemia and the innate immune system: clinical, cellular, and molecular aspects. *Crit Care Med* 33: 1624–1633. <https://doi.org/10.1097/01.ccm.0000170106.61978.d8>
62. Mowat A and Baum J (1971) Chemotaxis of polymorphonuclear leukocytes from patients with diabetes mellitus. *N Engl J Med* 25: 621–627. <https://doi.org/10.1056/NEJM197103252841201>

63. Twigg SM, Chen MM, Joly AH, et al. (2001) Advanced glycosylation end products up-regulate connective tissue growth factor (insulin-like growth factor-binding protein-related protein 2) in human fibroblasts: a potential mechanism for expansion of extracellular matrix in diabetes mellitus. *Endocrinology* 142: 1760–1769. <https://doi.org/10.1210/endo.142.5.8141>
64. Gardiner M, Vicaretti M, Sparks J, et al. (2017) A longitudinal study of the diabetic skin and wound microbiome. *Peer J* 20: e3543. <https://doi.org/10.7717/peerj.3543>
65. Petrowsky H, Demartines N, Rousson V, et al. (2004) Evidence-based value of prophylactic drainage in gastrointestinal surgery: a systematic review and meta-analyses. *Ann Surg* 240: 1074–1084. <https://doi.org/10.1097/01.sla.0000146149.17411.c5>
66. Willett KM, Simmons CD, Bentley G (1988) The effect of suction drains after total hip replacement. *J Bone Joint Surg Br* 70: 607–610. <https://doi.org/10.1302/0301-620X.70B4.3403607>
67. Bassi C, Molinari E, Malleo G, et al. (2010) Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. *Ann Surg* 252: 207–214. <https://doi.org/10.1097/SLA.0b013e3181e61e88>
68. Shirata C, Hasegawa K, Kokudo T, et al. (2017) Surgical site infection after hepatectomy for hepatocellular carcinoma. *Digestive Surg* 35: 204–211. <https://doi.org/10.1159/000477777>



AIMS Press

© 2022 the Author(s), licensee AIMS Press. This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>)