Review

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

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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 accessed and thus was not included. A total of 16 papers were then eligible for use in this systematic review.
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 Algadossellés 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.

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Methods, Country</th>
<th>Surgery type(s)</th>
<th>Sample size</th>
<th>Total SSI</th>
<th>Laparoscopic</th>
<th>SSI definition</th>
<th>Superficial</th>
<th>Deep SSI</th>
<th>Superficial and organ space</th>
<th>Organ space</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laviano et al., 2020 [12]</td>
<td>Observational, prospective, Spain</td>
<td>Cholecystectomy, pancreaticoduodenectomy, total pancreatectomy, segmentectomy, hepatectomy, hepaticojejunostomy and exploratory laparotomy</td>
<td>321</td>
<td>25.80%</td>
<td>35%</td>
<td>NR</td>
<td>4%</td>
<td>4%</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>Joliat et al., 2018 [13]</td>
<td>Observational, retrospective, Switzerland</td>
<td>Pancreatic</td>
<td>529</td>
<td>26%</td>
<td>NR</td>
<td>CDC</td>
<td>48.60%</td>
<td>NR</td>
<td>34.70%</td>
<td>16.70%</td>
</tr>
<tr>
<td>Algado-Sellés et al., 2022 [14]</td>
<td>Observational, prospective, cohort, Spain</td>
<td>Cholecystectomy</td>
<td>2,200</td>
<td>5%</td>
<td>88.70%</td>
<td>CDC</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Bortolotti et al., 2021 [17]</td>
<td>Observational, retrospective, monocentric, France</td>
<td>Pancreaticoduodenectomy</td>
<td>129</td>
<td>14.80%</td>
<td>0%</td>
<td>CDC</td>
<td>100%</td>
<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>First author, year</th>
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<th>Sample size</th>
<th>Total SSI</th>
<th>Laparoscopy</th>
<th>SSI definition</th>
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<th>Deep SSI</th>
<th>Superficial and organ space</th>
<th>Organ space SSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liu et al., 2019 [18]</td>
<td>Observational, cohort, USA Pancreatoduodenectomy</td>
<td>5969</td>
<td>20.30%</td>
<td>0%</td>
<td>CDC</td>
<td>7.20%</td>
<td></td>
<td>14.10%</td>
<td></td>
</tr>
<tr>
<td>Sert et al., 2022 [20]</td>
<td>Observational, Turkey Pancreatoduodenectomy</td>
<td>45</td>
<td>40%</td>
<td>0%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gyoten et al., 2021 [21]</td>
<td>Observational, prospective, Japan Pancreatoduodenectomy, 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</td>
<td>66</td>
<td>30.30%</td>
<td>0%</td>
<td>CDC</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Bednarsch et al., 2021 [23]</td>
<td>Observational, cohort, Germany Liver resection with mandatory portal vein reconstruction (and hepatoduodenalpancreatectomy on demand)</td>
<td>95</td>
<td>54.70%</td>
<td>0%</td>
<td>Postoperative abdominal infection</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

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<th>Superficial and organ space</th>
<th>Organ space SSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wagle et al., 2020 [24]</td>
<td>Retrospective, observational</td>
<td>India</td>
<td>Hepatectomy</td>
<td>19</td>
<td>36.80%</td>
<td>0%</td>
<td>CDC</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Herzog et al., 2015 [25]</td>
<td>Retrospective, observational, cohort</td>
<td>Germany</td>
<td>Pancreatic head resection or palliative bypass procedures</td>
<td>887</td>
<td>10%</td>
<td>NR</td>
<td>CDC</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Li et al., 2017 [26]</td>
<td>Observational, retrospective</td>
<td>China</td>
<td>Hepatectomy combined with hepaticojejunostomy</td>
<td>335</td>
<td>10.15%</td>
<td>0%</td>
<td>CDC</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Bhayani et al., 2014 [27]</td>
<td>Observational, retrospective</td>
<td>USA</td>
<td>Pancreatectoduodenectomy, total pancreatic resection</td>
<td>6512</td>
<td>19.30%</td>
<td>0%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gavazzi et al., 2016 [28]</td>
<td>Observational, retrospective</td>
<td>Italy</td>
<td>Pancreatectoduodenectomy</td>
<td>178</td>
<td>20.80%</td>
<td>NR</td>
<td>CDC</td>
<td>11.80%</td>
<td>9%</td>
<td>26.80%</td>
<td></td>
</tr>
<tr>
<td>Rodríguez-Caravaca et al., 2016 [30]</td>
<td>Observational, retrospective</td>
<td>Spain</td>
<td>Cholecystectomy</td>
<td>766</td>
<td>1.96%</td>
<td>77%</td>
<td>NR</td>
<td>0.91%</td>
<td>0.52%</td>
<td>0.52%</td>
<td></td>
</tr>
</tbody>
</table>

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<th>Superficial SSI</th>
<th>Deep SSI</th>
<th>Organ space SSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodríguez-Sanjuán et al., 2013 [31]</td>
<td>Observational, prospective</td>
<td>Spain</td>
<td>Cholecystectomy</td>
<td>287</td>
<td>8.40%</td>
<td>73.90%</td>
<td>CDC</td>
<td>5.20%</td>
<td>3.10%</td>
<td></td>
</tr>
<tr>
<td>Comajuncosas et al., 2014 [33]</td>
<td>Observational, prospective</td>
<td>Spain</td>
<td>Cholecystectomy</td>
<td>220</td>
<td>17.70%</td>
<td>100%</td>
<td>CDC</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>De Pastena et al., 2018 [34]</td>
<td>Observational, retrospective</td>
<td>Italy</td>
<td>Pancreaticoduodenectomy</td>
<td>387</td>
<td>18%</td>
<td>NR</td>
<td>Clavien–Dindo classification</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Huang et al., 2015 [36]</td>
<td>Observational, retrospective</td>
<td>China</td>
<td>Pancreaticoduodenectomy</td>
<td>270</td>
<td>35.60%</td>
<td>NR</td>
<td>Clavien–Dindo classification</td>
<td>16.60%</td>
<td>NR</td>
<td>18.90%</td>
</tr>
</tbody>
</table>
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).
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).](image)

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).](image)
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.

![Forest plot of odds ratio of smoking status and SSI (95% CI).](image)

**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%).

![Forest plot of odds ratio of diabetes and SSI (95% CI).](image)

**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).

![Forest plot of odds ratio of preoperative biliary stent and SSI (95% CI).](image)

**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 [pancreatoduodenectomy (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.

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

Continued on next page
First Author, year | Three most commonly reported organisms of SSIs | Key risk factors of SSIs
--- | --- | ---
Herzog et al., 2015 [25] | Enterococcus spp. (41%)  
E. coli (17%)  
MRSA (12%) | Positive bile duct cultures
Li et al., 2017 [26] | E. coli (25%), S. epidermidis (12.5%),  
Pseudomonas spp./Streptococcus 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) Enterococcus spp. (69.1%),  
E. coli (26.8%),  
Staphylococcus spp. (26.8%) | BMI ≥25 kg/m2, biliary stenting, cardiac disease
Rodriguez-Caravaca et al., 2016 [30] | E. coli (47.8%), Klebsiella pneumoniae (13.1%).  
E. faecium (13.1%) | Open surgery, renal failure, diabetes mellitus, malignancy, chronic obstructive pulmonary disease, liver cirrhosis, obesity, neutropenia, neoplasia
Rodriguez-Sanjuán et al., 2013 [31] | E. coli (26.5%), Streptococcus spp. (19.4%), Enterococcus spp. (17.3%) | Open surgery, conversion to open surgery
Comajuncosas et al., 2014 [33] | NR | NR
De Pastena et al., 2018 [34] | (Bile cultures) E. coli (19.9%),  
E. faecalis (18.8%), Klebsiella 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 metaanalysis 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 supress 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


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