JOURNAL OF HEALTHCARE SCIENCES
Volume 2 Issue 10 2022, Article ID: JOHS2022000518
http://dx.doi.org/10.52533/JOHS.2022.21004
e-ISSN: 1658-8967

Review

Surgical Site Infection in Patients Undergoing Potentially Curative Surgery for Colorectal Cancer in Saudi Arabia: A Systematic Review

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Received: 28 September 2022, Revised: 3 October 2022, Accepted: 8 October 2022, Published: 14 October 2022

Abstract

Colon cancer is the third most common cancer worldwide and its incidence is increasing day by day. Colorectal cancer surgeries can have many complications including surgical site infection (SSI). SSI in colorectal cancer has been a serious healthcare problem due to the delay in postoperative recovery. Our present study aimed to explore the rate of SSI and associated factors in colorectal cancer in Saudi Arabian patients. Relevant literature was searched in multiple databases, including PubMed/Medline, Google Scholar, and the Cochrane Library. We included original investigation analyses of more than 10 cases that met the inclusion criteria. The SSI rate, wound infection rate, other post-procedure complications, and risk factors for SSI were extracted from the selected articles. A total of 9 studies that recruited a total of 2,889 patients who underwent the colorectal open or laparoscopic procedure with post-procedure infectious complications reported were included in this review. Every single study that was incorporated was an observational study, such as a cross-sectional or cohort. Most of the included studies had a retrospective design. Of the total patients, 53.34% (n = 1541) were male patients. The age of the patients in the studies included ranged from 18 to 93 of age. The overall surgical site infection rate of included studies from Saudi Arabia was 12%. The highest infection rate was observed in open colorectal surgeries compared to laparoscopic surgeries. Further research is needed to understand both the associated risk factors and the infectious post-surgical consequences. Optimal precautions and standard surgical techniques are required to support the actions of the surgical team to reduce SSI occurrence and to decrease such complication.

Keywords: colorectal cancer, surgical site infection, Saudi Arabia, systematic review, prevalence, complication rate.

Introduction

Surgical site infections (SSI) refer to an infection occurring at or near a surgical incision within 30 days of an operation or 1 year of the implantation of a foreign body and are among the most preventable health-care-associated infections and are a substantial burden to healthcare systems and service payers worldwide in terms of patient morbidity, mortality, and additional costs. In addition, they are associated with potential delays in, or omission of, adjuvant therapy. The majority of infections related to healthcare are SSIs, according to the World Health Organisation. Surgical site infection is divided into two categories by the US Centers for Disease Control and Prevention (CDC): superficial wound infection and deep organ/space infection, including anastomotic leak and abscess (1). The incidence of colorectal cancer surgery SSI was reported to be between 23% and 38% (2-4). Oncological and general outcomes were linked to surgical complications in colorectal cancer. Biological factors affect post-surgical survival after resection (5). An understanding of potential negative relationships is crucial because SSI affects 15% of individuals having colorectal surgery (6).

In Saudi Arabia, colorectal cancer has the highest incidence in males and the third highest in females (7). In colorectal cancer, surgical resection remains the primary treatment, and resection may be associated with some appreciable morbidity and mortality. Colorectal surgery is considered to have the highest SSI rate (8). It sometimes results in mortality and is linked to higher treatment costs and longer hospital stays (8, 9). The oncological outcome of colorectal cancer, surgical quality, and patient safety can all be adversely affected by SSI, a common postoperative complication of colorectal cancer surgeries. Inpatient morbidity and costs are strongly and independently correlated with length of hospital stay (LOS) and surgical site infections (10). To effectively reduce the frequency of postoperative infection among high-risk groups, it is, therefore, crucial to identify risk factors for SSI in colorectal cancer (11).

Previous studies identified multiple factors for the development of SSIs in colorectal surgeries, such as American Society of Anesthesiologists (ASA) score, cigarette smoking, systemic steroid use, obesity, extremes of age, poor nutritional status, tumor location, and serum albumin level (12, 13), surgery duration, stoma formation, open surgery, and blood transfusion (13). The type of antibiotic prophylaxis used is considered one of the most important methods to reduce the risk of SSIs. Even if prior systematic studies investigated the post-surgical infection rate and its risk factors, they did not include studies from Saudi Arabia. Hence, in this present study, we aimed to investigate the SSI rate of colorectal cancer surgery in the Saudi Arabian population. A systematic review was undertaken to determine the SSI rate and risk factors for SSI and other post-procedure complications in colorectal cancer surgery.

Methods

Definition of outcomes and inclusion criteria

The primary outcome of this review was to analyze the rate of surgical site infection or wound infection. Secondly, we investigated the other complications and risk factors of the post-procedure complications. This study was conducted according to the preferred reporting items for systematic review guidelines. All published cohort or cross-sectional studies that investigated post-operative SSI complications in Saudi Arabia were included in this systematic review. Studies with fewer than 10 patients, case reports, studies that included cases with colorectal surgery that was not due to carcinoma, and studies that included a variety of gastrointestinal cancers were excluded.

Search strategy

An extensive electronic database search was performed using PubMed/Medline, Google Scholar, and the Cochrane Library to identify the published research articles collected after 1995. Based on our determined outcomes, we retrieved the relevant keywords from a brief manual screening within the potentially included studies to design the most suitable search term. We used the following keywords in free text and medical subject heading (MeSH) “surgical site infection” AND “postoperative complications” AND “Saudi Arabia” OR “surgical site infection OR wound infections” AND colorectal “cancer OR neoplasms” AND “Saudi Arabia”. A search of the bibliographies of selected papers was carried out to identify any relevant articles missed during the primary search. Our search strategy was limited to the title and abstract of the search results to utilize all the relevant studies only. Also, we filtered studies conducted only in Saudi Arabia. All these results were exported to an Endnote library to identify and execute all duplicates between the different searched databases. Furthermore, we manually searched all similar article sections in PubMed and the references of the included studies and relevant reviews for possible detection of any missed studies by the main electronic search strategy. All steps

http://dx.doi.org/10.52533/JOHS.2022.21004

of this systematic review were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (14).

Screening and extraction

We used a double screening strategy, one for screening titles and abstracts and the other for screening full texts, to maintain high quality in this important process. After ensuring that all relevant articles were included, an extraction sheet was constructed in an organized way relevant to our aimed outcomes. The sheet was composed of the baseline characteristics and the sought outcomes. For each study, data on study characteristics (including the year of publication, country of origin, design, sample size, cancer site, surgical approach), surgical site infections or wound infections, additional risk factors for SSI, and other post-op complications were extracted and entered into pre-built tables.

Quality assessment

The quality and risk of bias of the included research were assessed using a modified Newcastle-Ottawa scale for evaluating the quality of nonrandomized observational studies (15). The original Newcastle-Ottawa scale for nonrandomized studies is used to evaluate the three main areas of selection, comparability, and outcomes. This scale gives each category a maximum of four, two, and three stars, respectively. The selection was assessed based on power estimates, sequential participant selection, and recruiting bias. Comparability was established using studies that included adjustments for either of the following variables: participant age (<40), gender, obesity, and open or laparoscopic procedure. It is widely accepted that a maximum of five stars could be used to distinguish studies with little risk of bias. Studies were rated as low (0-3), moderate (4-6), and high quality (7-9), on a scale of 0 to 9, depending on how biased they were.

Results

Search results

A total of 18 abstracts were screened from the 321 publications obtained using the aforementioned search strategy, with English as the only language. If abstracts were found relevant, the full-text article was reviewed. Of the 14 articles assessed, 9 met all the criteria for inclusion and were included and investigated in the review. A total of 9 studies with a total of 2889 patients fulfilled the inclusion criteria and are presented in the analysis **(Figure 1).**

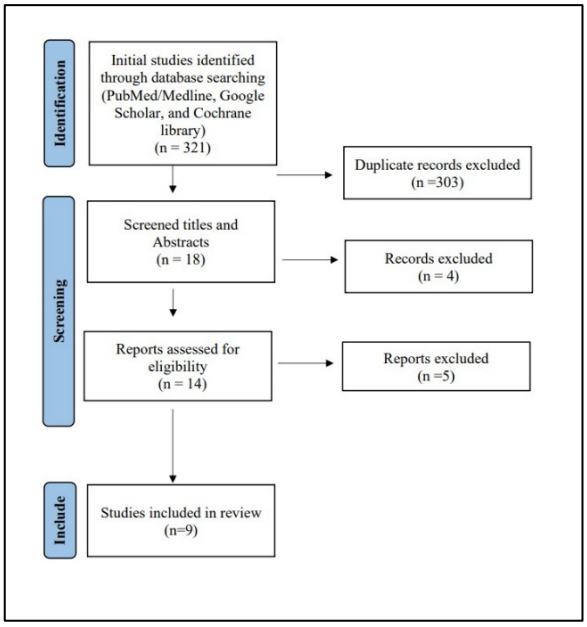

***Figure 1**: PRISMA flow chart showing the included articles*

Results of quality assessment

Our assessment of bias for the included studies showed that all the studies scored above five and most of the reviewed studies had moderate quality (n = 7), which was associated with a lower risk of bias. Two studies were of high quality. None of the included studies showed low quality **(Table 1).**

Table 1. Summary of the results of bias assessment of the included studies using the modified Newcastle-Ottawa scale (NOS) for non-randomized observational studies.

Study	Selection	Comparability	Outcome	Total Score	Study Quality
Meshikhes et al.	***	*	**	6	moderate
Eltinay OF et al.	***	*	**	6	moderate
Hakami et al.	***	**	*	6	moderate
Hibbert D et al.	***	*	**	6	moderate
Almasaudi AS et al.	***	**	*	6	moderate
Abdullah A et al.	***	**	**	7	high
Alkhayal KA et al.	***	**	**	7	high
Masoud et al.	***	*	**	6	moderate
Malibary N et al.	***	*	**	6	moderate

http://dx.doi.org/10.52533/JOHS.2022.21004

Characteristics of the study included

We examined 9 studies that collected data between 1995 and 2019 and enrolled a total of 2889 subjects (16-24). All the included studies are from Saudi Arabia. All the included studies were observational studies such as cross-sectional and cohort, either prospective or retrospective. Most of the included studies were retrospective in nature. Of the total patients, 53.34% (n = 1541) were male patients. The age of the patients ranged from 18 to 93. Seven studies recruited both colorectal procedures (16, 17, 19-21, 23, 24), while two studies included only colon cancer patients (18, 22). Three of the included studies recruited patients who underwent open surgery or laparoscopic (18, 22, 24). The overall surgical site infection rate of included studies from Saudi Arabia was 12%. The highest infection rate was observed in open colorectal surgeries compared to laparoscopic surgeries. Risk factors for the development of SSI were reported in two included studies. All the baseline characteristics of the study included in the review are shown in **Table 2.**

Table 2. Baseline characteristics of the included studies in this review.

Study	Data collection period	Study type and design	Sample size	Age	Gender(M/F)	Type of surgery	Tumor location
Meshikhes et al.	1995 -1996	retrospective observational	23	[a]45 (15-75)	15/6	open	colorectal
Eltinay OF et al.	1999 - 2003	retrospective observational	43	[a]42.7 (23-79)	33/10	open	colorectal
Hakami et al.	2000 - 2015	retrospective cohort	721	[a]57.8	378/343	open and laparoscopic	colon
Hibbert D et al.	2013	prospective observational	296	[a]53.9 (19 – 93)	159/137	open colorectal	colorectal
Almasaudi AS et al.	1997 - 2016	retrospective observational	1039	65 = 206, 65-75 = 233, >75 = 148	587/442	laparoscopic	colorectal
Abdullah A et al.	2010 - 2014	retrospective observational	72	[a]56.4 ± 15.1	45/27	open	colorectal
Alkhayal KA et al.	2009 - 2013	retrospective observational	65	[a]59.5 ±11.3	28/37	open and laparoscopic	colon
Masoud et al.	2019	cross-sectional	510	<25 = 214, >25 = 296	224/286	colorectal	colorectal
Malibary N et al.	2016 - 2019	retrospective cohort	120	[a]61.36 ± 13.85	72/48	open and laparoscopic	colorectal

[a] *Mean and standard deviation or range*

Discussion

As many as 30% of patients who underwent surgery in low- and middle-income countries had surgical site infections. Even in high-income countries, surgical site infections account for more than 25% of all diseases associated with medical care. Deep or organ space infections are very common post-operative infectious complications that are associated with higher expenses, higher recurrence, and lower long-term survival. This systematic review of 2889 patients in 9 studies evaluated the rate of SSI complications. Despite major advances in surgical procedures, surgical morbidity after colorectal cancer resection remains a significant problem, with infectious complications, particularly SSI. The results of the present systematic review showed that, overall, 12% SSI after colorectal cancer surgical procedures in Saudi Arabia. In the current systematic review, we also analyzed the risk factors of surgical site infection in a patient undergoing surgery for colorectal cancer. There have been other systematic reviews and meta-analyses in this area. However, those studies did not include the research studies from Saudi Arabia which addressed the surgical site infection following colorectal cancer surgery.

Obesity, age, and prealbumin level are all independent risk factors for SSI postoperative infective complications. Other common complications included anastomosis leak, pneumonia, Urinary tract infection (UTI), deep vein thrombosis, ileus, bleeding, and atelectasis. Surgical site infection and wound infection were lower in laparoscopic surgery methods than in open surgery. In a meta-analysis, Shabanzadeh *et al.* (25) concluded that laparoscopic surgery in obese patients reduces surgical site infection rates by 70% - 80%

http://dx.doi.org/10.52533/JOHS.2022.21004

compared with open surgery across general abdominal surgical procedures. This may be due, in part, to the longer and deeper wounds, with associated greater dead space, required for open surgery on obese patients. Also, Fuji *et al.* (26) reported lower odds of incisional surgical site infection in laparoscopic approaches compared to open surgical procedures (OR = 0.6262, 95%CI: 0.4310-0.9097, *P* = 0.0140). Prior meta-analysis results are in line with our included study findings (26, 27). In this present review, Malibary *et al*. (24) reported a higher percentage (87.5%) of SSI in open surgery than in closed. The average age of the patients was 61.36 ± 13.85. A higher mean age may be a significant reason for the higher SSI rate in their study. However, only three of the patients who underwent laparoscopic surgery had SSI. This indicates that laparoscopic procedures in older patients resulted in a low infection rate. However, also, Hibbert *et al*. (19) conducted a prospective observational longitudinal study in a tertiary referral center in Saudi Arabia and reported 30% of abdominal incision infections after elective open colorectal surgery. Hakami *et al*. (18) did not find a significant difference in the wound infection rate between open and laparoscopic colorectal surgery procedures. However, there was a slight increase in the wound infection rate in open surgery patients (6.8% vs 6.9%). In addition, a better quality of life was observed in patients that underwent laparoscopic colectomy in a randomized controlled trial. Another study conducted between 2007 and 2016 claimed that gram-negative pathogens were a significant contributor to surgical site infection in multiple Saudi health care systems. According to the findings of the study, Saudi Arabia is responsible for more than 60% of all SSIs with more resistant patterns than western countries (28). In procedures with non-clean wounds, *Escherichia coli* was the most frequent pathogen in colorectal surgeries (28). Masoud *et al*. (23) studied most of the patients who were 18–35 years of age and reported that 80.4% had no complications and only 3.9 percent presented with SSI. A cross-sectional study conducted during the 90s period in Saudi Arabia by Isbister *et al*. (29) observed that leaking anastomoses were associated with more wound infections (65.5% vs 14.8%) and that in patients who developed a leak after the same operation, the mortality rate was 24.1% after colorectal resection **(Table 3)**.

Table 3. Summary of the outcomes of the included studies in this review.

Study	Rate of infection	Risk factors	Other complication
Meshikhes et al.	2 (8.70%)	NR	intra-abdominal collection, anastomotic leak
Eltinay OF et al.	5 (11.6%)	NR	anastomotic leak, deep vein thrombosis
Hakami et al.	overall = 92 (12.76%) open=49 (6.8%) laparoscopic = 43 (5.9%)	NR	intra-abdominal collection, bleeding, wound dehiscence, anastomotic leak, stenosis
Hibbert D et al.	89 (30%)	BMI, pre-albumin level	anastomotic leak, other organs/space infection
Almasaudi AS et al.	104 (10.01%)	BMI, age	anastomotic leak
Abdullah A et al.	4 (5.56%)	NR	Intestinal obstruction, sepsis, DVT, Anastomotic leak, hydronephrosis
Alkhayal KA et al.	6 (9.23%)	NR	Post-operative ileus, UTI, pneumonia, deep vein thrombosis
Masoud et al.	20 (3.9%)	NR	Anastomotic leak, ileus, bleeding
Malibary N et al.	overall = 20% open= 21 (87.5%), laparoscopic = 3 (12.5%)	NR	Anastomosis leak, pneumonia, UTI, DVT, Atelectasis

NR: Not reported, BMI: Body Mass Index; UTI: Urinary Tract Infection; DVT: Deep vein thrombosis

Almasudi *et al.* (20) investigated the relationship and identified the risk factors for post-procedural complications in patients who underwent laparoscopic colorectal procedures. Their study population's majority was over the age of 65. In their study, men had a higher rate of complications (44%), particularly infective complications. Infectious problems affected 160 of these male patients (29%), while non-infectious complications affected 104 (9%). When complications were evaluated between BMI categories, there was a substantial link between BMI and the likelihood of wound infection and surgical site infection. Male patients with normal BMI had a 12% rate of surgical site infection, compared to 26% in those with a BMI ≥ 30 ($p < 0.001$). Wound infection was 7% in females with normal BMI compared to 20% in those with BMI ≥ 30 ($p < 0.001$). In females, it was significantly associated with higher BMI ($p < 0.001$); wound infections

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(p<0.001). Wound infection occurred in 6% of female patients with a normal BMI compared to 8% of those with a BMI of ≥ 30 (p = 0.003). The rate of surgical site infection in female patients was 10% with a normal BMI and the same in those with a 178 BMI ≥30 (p = 0.054). As per their findings, obesity increases the risk of post-op complications. Male obese patients should be considered at high risk of developing post-operative infective complications. Increased BMI in male patients was associated with a greater risk of SSIs and wound infection compared to female patients. It is noteworthy that a previous meta-analysis by Almasaudi *et al.* (30) found strong evidence linking obesity to a considerably greater risk of surgical site infection following colon cancer surgery in Asian nations. They found that the estimated pooled OR demonstrated that obesity increased the risk of surgical site infection by approximately 100% (OR = 2.13; 95% CI 1.66- 2.72, p< 25 vs ≥ 25 kg/m² was used to examine the association between obesity and surgical site infection. Another meta-analysis conducted by Zhou *et al.* (31) showed a significantly higher rate of wound infection in the obese compared with the nonobese group (9.6% vs. 2.6%). By several proposed mechanisms, obesity can increase the risk of wound infection by several proposed mechanisms, such as technical difficulties, tissue trauma, decreased circulation and decreased oxygenation, immune impairment, deficiencies in collagen synthesis, and inadequate tissue antibiotic concentrations (32, 33). It has been suggested that the use of subcutaneous drains (34) and subcutaneous retention sutures (35) increases overall dosing and broadens the spectrum of antibiotics (36) or that the infusion of topical antibiotics (37) may reduce the incidence of postoperative wound complications in obese patients.

According to Hibbert *et al.* (19) pre-operative pre-albumin (p = 0.02, OR 0.76, 95% CI 0.60–0.96), and obesity measured by BMI (p = 0.001, OR 4.71, 95% CI 2.20–10.10) were the significant risk factors for SSI. A review explained that anastomotic leakage and wound infection can occur only with severe degrees of malnutrition. Malnutrition exerts an adverse effect on tissue healing by affecting processes such as collagen synthesis or synthesis of sulphated mucopolysaccharides or affecting fibroblast proliferation (38). Many risk factors identified in other international studies were not found to be associated with SSI in the included studies in this review from Saudi Arabia: diagnosis and prospectively designed protocol (39, 40), ASA scores (41-43), advanced cancer (44), pre-operative radiation (4), presence of a stoma (45, 46), duration of surgery (45), surgeon (47), contaminated or dirty wound classification (46), and steroids (4, 45).

Colorectal cancer incidence and related mortalities have been steadily increasing in Saudi Arabia over the past 20 years, and surgical resection remains the primary treatment, which highlights the importance of a better understanding of post-op complications. The other post-op complications reported in the present SR are anastomotic leak, organ/space infection, post-operative ileus, UTI, pneumonia, and deep vein thrombosis. Our review of studies from Saudi Arabia indicates that the infection rate varied in different study centers and an overall higher percentage of SSI has been found. SSIs in this study's population may have been more common with the use of open surgery. We found that rates of laparoscopy continued to vary significantly across hospitals. Other risk factors, such as gender, age, and obesity, may also play a role. We do not assert that each of these infections would have been avoided simply by changing the surgical approach because many other patient-level factors may contribute to SSI risk. Future research examining the risk factor for post-procedure infectious complications and comparing open and laparoscopic approaches is required.

Evaluating surgical outcomes and comparing all healthcare facilities to best-standard benchmarks are crucial for ensuring the quality and safety of health services. Although measuring SSI in open and laparoscopic procedure complications is of paramount importance, it is particularly vital to determine surgical outcomes, LOS, and hospital costs for which several mechanisms and programs can be used. Also, increasing training and preference for laparoscopic approaches may modify SSI risk to a greater capacity than previously thought, especially in patients with multiple comorbidities who currently tend to undergo open procedures in many hospitals.

In addition, although the CDC has published definitions for surgical site infection, to allow more accurate recording and comparison, two included studies used more traditional descriptive methods of recording surgical site infection, e.g. "wound infection." Again, this lack of standardization in the definitions used may introduce errors in the pooled proportion. Furthermore, the overall rate of surgical site infection in the included observational studies was perhaps lower than expected following colorectal surgery, suggesting an element of selection bias. The other limitation is that most of the included studies were retrospective in nature and included a small number of patients. The main limitation

http://dx.doi.org/10.52533/JOHS.2022.21004

of the present systematic review was that it was based on observational studies, which led to several potential biases. Not all studies analyzed the risk factors of SSI.

Conclusion

Saudi Arabia had an overall rate of 12% SSI in colorectal cancer surgery. However, further research is needed to understand both the associated risk factors and the infectious post-surgical consequences. Optimal precautions and standard surgical techniques are required to support the actions of the health teams to reduce SSI occurrence and to decrease its complications if it occurs.

Disclosure

Conflict of interest

There is no conflict of interest

Funding

No funding

Ethical consideration

Non applicable

Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection, analysis and final writing of the manuscript.

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