



Systematic review and meta-analysis of the risk factors of surgical site infection in patients with colorectal cancer

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Background: Surgical site infection (SSI) influenced the result of surgical treatment, which was known as the second most prevalent hospital-based infection. But, the factors of SSI are not uniform. The purpose of this study was to identify the risk factors of SSI in patients with colorectal cancer. We conducted a meta-analysis of epidemiological research to provide a scientific basis for the prevention of SSI.

Methods: The PubMed, Medline, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang databases were independently searched by 2 researchers to identify all relevant studies. Studies were selected if they met the selection criteria, which was defined according to the PICOS principles. The quality of the evidence was assessed using Egger's P value, study heterogeneity, and sample size. Studies were categorized into 3 groups as follows: low quality (Class 4), moderate quality (Class 2/3), and high quality (Class 1). The meta-analysis was performed using RevMan 5.3 software.

Results: A total of 17 studies involving 61,611 patients were included in the meta-analysis. The results identified 7 patient-related risk factors of SSI, including male gender, obesity, diabetes mellitus, American Society of Anesthesiologists (ASA) score, cigarette smoking, tumor location, and serum albumin level, and 5 treatment-related risk factors, including laparoscopic surgery, operation time, blood loss, blood transfusion, and abdominal surgical history. Age was not directly related to SSI in colorectal cancer.

Conclusions: It is possible that patients can be treated effectively by identifying these factors of SSI.

Keywords: Colorectal cancer; surgical site infection (SSI); risk factors; meta-analysis

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Introduction

Surgical site infection (SSI) (1-3) refers 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. SSIs can be classified into 3 types: superficial incisional infection, deep incisional infection, and organ/space infection. The incidence rate of SSI differs according to the type of surgery, and studies have reported that the incidence

of SSI in colorectal cancer surgery is between 23% and 26% (4,5).

Colorectal cancer is a common gastrointestinal tumor (6). In 2012, colorectal cancer ranked third for incidence among men and second among women, with approximately 1.4 million new cases and about 690,000 deaths, making it the fourth most deadly cancer worldwide (7). In recent years, the incidence and mortality rates of colorectal cancer in China have increased alongside accelerating economic

development and urbanization and the changing dietary structure and living habits of residents (7). In 2012, the incidence and mortality rates of colorectal cancer in China were 0.83 times and 0.88 times that of the world and 1.03 times and 1.02 times that of Asian countries, respectively, with colorectal cancer ranking second among malignant tumors of the digestive system (7).

Surgery is the most important treatment for colorectal cancer, with nearly 90% of colorectal cancer patients receiving tumor resection. As a common postoperative complication of colorectal cancer surgery, SSI can seriously impact surgical quality and patient safety. One study found that patients with local disease were more likely to gain incisional infection, while patients with severe disease were more likely to gain organ/space infection (8), which can develop into systemic infection, septic shock, or multiple organ dysfunction syndrome. The high incidence of SSIs after colorectal cancer surgery has been increasingly recognized (9). Therefore, it is necessary to identify risk factors of SSI in colorectal cancer so that effective measures can be taken to reduce the incidence of postoperative infection among high-risk groups (9).

The occurrence of SSI in patients undergoing colorectal cancer surgery is influenced by many factors, including patient-related factors [age, obesity, diabetes mellitus, American Society of Anesthesiologists (ASA) score, cigarette smoking, tumor location, and serum albumin level], treatment-related factors (laparoscopic surgery, operation time, blood loss, blood transfusion, and abdominal surgical history), and medical environment-related factors (operating room ventilation, hand hygiene of medical staff, and disinfection of medical instruments) (10). Unsatisfactorily, few risk factors are generally accepted and some findings on these factors in medical literature are often contradictory.

The purpose of this study was to explore the risk factors of postoperative SSI in patients with colorectal cancer and to provide a scientific basis for the formulation of preventive measures against SSI. We present the following article in accordance with the MOOSE reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-627/rc>) (11).

Methods

Publication search

The PubMed, Medline, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang databases

were searched from inception to 2021 by 2 reviewers. All literature in the databases was searched without language restrictions. The search terms were as follows: (“Colorectal, rectal, colon, or colorectal cancer”); (“colon, surgical infection, risk, or site”); (“colorectal tumor, site infection, risk factors, or wound infection”); (“colon, infection, risk factors, or wound infection”); (“colorectal cancer, surgery, wound infection, or risk”). The reference list of each included study was also explored to identify other high-quality research.

Selection of studies

The inclusion criteria were formulated based on the PICOS (population, intervention, comparator, outcomes, and study design) framework (12). These criteria were as follows: patients had undergone colorectal surgery; relevant interventions were performed on patients; the incidence of risk factors was shown by odds ratios (ORs) or relative risks (RRs) with corresponding 95% confidence intervals (CIs); and the studies were case-control or cohort studies.

The following types of literature were excluded: reviews, study protocols, letters, conference abstracts, unpublished papers, animal experiments, and studies with insufficient data.

Data extraction and quality assessment

The 2 investigators independently performed the data extraction according to pre-agreed criteria. When there was a disagreement, this was resolved through discussion with a third investigator. The ORs and corresponding 95% CIs were chosen for analysis in this review. Cross-sectional studies on the prevalence and associated factors of SSI were excluded, because of the small sample number. The data extracted from each study were as follows: the first author, year of publication, country, recruitment period, sample size, type of SSI, study type, location of tumor, risk factors, and Newcastle-Ottawa scale (NOS) score (13).

The quality assessment was performed according to the 3 dimensions of NOS: (I) selection of study groups; (II) intercomparability of the study; and (III) outcomes (14). The highest NOS score is 9 stars, and studies scoring 7 stars were considered to be of high quality (13). The relevant results are shown in *Table 1*. In addition, the strength of the evidence was assessed using the following 3 indicators: (I) a total sample size of more than 1000; (II) intergroup inconsistency (I^2) of less than 50%; and (III) an Egger's P value of more than 0.1 (*Table 2*). Studies were considered

Table 1 The quality assessment of included studies by the NOS

Study	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Yu Tang 2020	1	1	1	1	1	1	1	1	8
Jung Wook Huh 2019	1	1	1		1	1	1	1	7
Takatoshi Nakamura 2016	1	1	1		1	1	1	1	7
Toshimichi Tanaka 2017	1	1	1	1	1	1	1	1	8
Joseph Drosdeck 2013	1	1	1	1	1	1	1	1	8
Kenji Katsumata 2021	1	1	1		1	1	1	1	7
Keita Itatsu 2014	1	1	1		1	1	1	1	7
Takatoshi Nakamura 2020	1	1	1	1	1	1	1	1	8
Thibault Crombe 2016	1	1	1		1	1	1	1	7
Chikao Miki 2006	1	1	1		1	1	1	1	7
Sam E. Mason 2017	1	1	1		1	1	1	1	7
Avinash Bhakta 2016	1	1	1		1	1	1	1	7
Marta Silvestri 2018	1	1	1		1	1	1	1	7
Wick EC 2011	1	1	1		1	1	1	1	7
Masanori Watanabe 2015	1	1	1	1	1	1	1	1	8
Mary R. Kwaan 2013	1	1	1		1	1	1	1	7
Tolga Olmez 2020	1	1	1		1	1	1	1	7

NOS, Newcastle Ottawa scale.

Table 2 Risk factors of SSIs in patients undergoing CRS

Significant factors	No. of studies	No. of patients	I ² (%)	P _{Begg-Mazumdar's}	OR (95% CI)	Evidence grading
Male gender	10	55,706	28	0.19	1.20 (1.08, 1.35)	Class 1
Obesity	12	58,648	94	<0.0001	1.38 (1.20, 1.60)	Class 3
Diabetes mellitus	8	48,804	0	0.43	1.58 (1.44, 1.72)	Class 1
ASA score	6	6,111	0	0.78	1.72 (1.39, 2.12)	Class 1
Laparoscopic surgery	3	2,608	42	0.18	1.95 (1.20, 3.16)	Class 1
Cigarette smoking	5	44,588	0	0.77	1.35 (1.28, 1.43)	Class 1
Operation time	9	49,624	69	0.001	2.05 (1.61, 2.59)	Class 3
Age	10	56,525	83	0.36	0.98 (0.93, 1.03)	Class 2
Blood loss	3	926	80	0.007	1.38 (0.72, 2.66)	Class 4
Blood transfusion	4	4,993	0	0.56	2.02 (1.48, 2.77)	Class 1
Tumor location	4	4,770	66	0.03	1.16 (0.72, 1.86)	Class 3
Serum albumin	3	2,263	0	0.91	3.36 (2.25, 5.02)	Class 1
Ostomy formation	3	1,328	0	0.56	0.74 (0.50, 1.11)	Class 1
Abdominal surgical history	3	1,849	0	0.46	1.64 (1.18, 2.28)	Class 1

SSIs, surgical site infections; CRS, colorectal Surgical; P value, probability value; 95% CI, 95% confidence interval; OR, odds ratio; ASA, American Society of Anesthesiologists.

to have high-quality evidence when they satisfied all 3 indicators (Class 1), moderate-quality evidence when they satisfied 2 indicators (Class 2) or 1 indicator (Class 3), and low-quality evidence when they satisfied none of the indicators (Class 4).

Statistical analysis

Statistical analyses were conducted by 2 investigators using RevMan version 5.3 (Cochrane, London, UK). The summary ORs and 95% CIs of the studies were analyzed using the DerSimonian-Laird random-effects model. OR values of the same factor from different studies were directly pooled when the P value was less than 0.05. The intergroup heterogeneity of each study was evaluated according to Cochran's Q (χ^2) test, which was quantified with the I² statistic. Heterogeneity was assessed using 3 risk levels based on the I² value (low I²<50%, moderate I²=50–74%, and high I²>75%). A sensitivity analysis was performed, and the effect model was changed to identify potential sources of heterogeneities. Publication bias was evaluated using funnel plots, and funnel plot asymmetry was further corrected using the trim and fill method.

Results

Study characteristics

A total of 1,189 studies were retrieved from the databases and screened independently by 2 investigators. A total of 986 references remained after exclusion of duplicates. A further 534 studies were excluded after reading the topics or abstracts. Finally, 17 studies (10,14–29) were enrolled in this meta-analysis after a full-text review by the 2 investigators. The patients in the included studies had undergone colorectal cancer surgery, and the risk factors of SSI were included in each study. The relevant baseline characteristics of the patients in the included studies are shown in *Table 3*. The process of literature retrieval is detailed in *Figure 1*.

Risk factors of SSI

A total of 33 risk factors were identified from the 17 included studies (10,14–29). Among these risk factors, 14 were reported in at least 3 studies (*Table 3*), and 19 were mentioned in fewer than 3 studies. To avoid bias in the results, only the 14 risk factors with a high incidence were selected in this study, and there was no further analysis of

Table 3 General characteristics of included studies

Author	Nation	Recruited period	Number of patients	Type of SSI	Study type	Location of tumors	Risk factors
Yu Tang 2020	China	April 2015–May 2017	326	SSIs	Cohort study	Colorectal cancer	12, 24
Jung Wook Huh 2019	South Korea	January 2009 to December 2011	3575	SSIs	Cohort study	Colorectal cancer	1, 2, 3, 4, 7, 8, 10, 11, 15, 16
Takatoshi Nakamura 2016	Japan	January 2010 through April 2015	670	SSIs	Cohort study	Colon cancer	4, 17
Toshimichi Tanaka 2017	Japan	January 1, 2012 to December 31, 2013	432	SSIs	Cohort study	Colorectal cancer	1, 2, 3, 4, 7, 8, 9, 10, 15, 18, 19, 20
Joseph Drosdeck 2013	USA	January 2006 and October 2012	419	SSIs	Cohort study	Laparoscopic colon resections	1, 2, 3, 5, 6, 8, 12, 21, 22, 23, 24, 25, 26
Kenji Katsumata 2021	Japan	–	701	SSIs	Cohort study	Rectal cancer	1, 2, 7, 8, 10, 11
Keita Itatsu 2014	Japan	November 2009–February 2011	1,980	I-SSI	Cohort study	Colorectal cancer	25, 27, 28
Takatoshi Nakamura 2020	Japan	January 2010–December 2017	1,144	SSIs	Cohort study	Colon cancer	18
Thibault Crombe 2016	France	2004–2013	1,104	SSIs	Cohort study	Colorectal cancer	2, 3, 6, 7, 8, 12
Chikao Miki 2006	Japan	–	285	SSIs	Cohort study	Colorectal cancer	1, 9, 10, 11, 30
Sam E. Mason 2017	UK	September 2012–July 2014	246	SSIs	Cohort study	Colorectal cancer	1, 2, 3, 6, 8, 29, 31, 32
Avinash Bhakta 2016	USA	2008–2012	42,132	SSIs	Cohort study	Colorectal cancer	1, 2, 3, 6, 8, 33
Marta Silvestri 2018	Italy	June, 2010–July, 2014	687	SSIs	Cohort study	Colorectal cancer	1, 2, 3, 4, 6, 7, 8, 17, 18, 19
Wick EC 2011	Maryland	January 1, 2002–December 31, 2008	7,020	SSIs	Cohort study	Colon cancer, diverticulitis, or inflammatory bowel disease	1, 2, 8
Masanori Watanabe 2015	Japan	2005–2010	538	SSIs	Cohort study	Colorectal cancer	4
Mary R. Kwaan 2013	Canada	2008–2009	143	SSIs	Cohort study	Colorectal cancer	2, 14
Tolga Olmez 2020	Turkey	January 2013–July 2019	209	SSIs	Cohort study	Colorectal cancer	1, 2, 3, 4, 5, 9, 11, 13, 19

1. male gender; 2. obesity (BMI >30 kg/m²); 3. diabetes mellitus; 4. ASA score ≥3; 5. laparoscopic surgery; 6. cigarette smoking; 7. operation time (≥180 min); 8. age ≥65 years; 9. estimated blood loss ≥100 mL; 10. blood transfusion; 11. tumor location; 12. abdominal surgical history; 13. peri-operative immunonutrition (no/yes); 14. midpoint from umbilicus to pubis; 15. clinical stage; 16. tumor size; 17. pre-hemoglobin >10 g/dL; 18. serum albumin, <2.5 g/dL; 19. ostomy formation; 20. blood flow preservation; 21. hand assistance; 22. Pfannenstiel incision; 23. prior open abdominal surgery; 24. history of COPD; 25. immunosuppressants; 26. postoperative chemotherapy; 27. chronic liver disease; 28. wound length; 29. wound classification; 30. concomitant medical problems; 31. conversion to open approach; 32. use of conditioned CO₂; 33. radiation. SSI, surgical site infection; I-SSI, incisional surgical site infection; BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

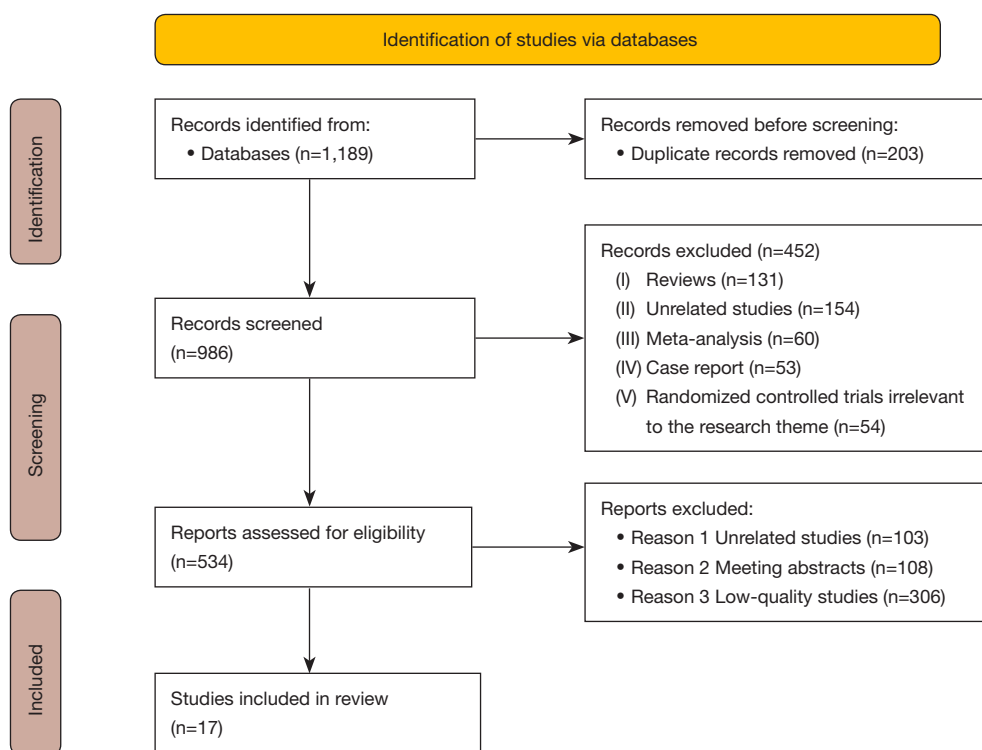


Figure 1 The flowchart of included studies.

the other 19 risk factors, of which the sample size was too small. The 14 selected risk factors were divided into patient-related risk factors and treatment-related risk factors.

Patient-related risk factors

Male gender

Male gender was reported in 10 of the 17 included studies (15,17-19,21,22,24,25,27,29). The results revealed a strong correlation between male gender and SSIs (OR =1.20, 95% CI: 1.08–1.35, $I^2=28\%$; *Figure 2*).

Obesity

Following the World Health Organization (WHO) classification, we defined obesity as a BMI over 30 kg/m². A total of 12 studies (10,15,17-22,24,25,27,30) found that patients with obesity may have a high risk of SSIs (OR =1.38, 95% CI: 1.20–1.60, $I^2=94\%$; *Figure 3*).

Diabetes mellitus

Eight studies (15-18,21,24,25,27) reported data suggesting that diabetes mellitus may influence SSI incidence. From these results, we concluded that there was a significant

positive relationship between diabetes mellitus and SSIs (OR =1.58, 95% CI: 1.44–1.72, $I^2=0\%$; *Figure 4*).

ASA score

Six studies (18,23-25,27,29) reported the ASA score of patients. An ASA score of more than 3 was related to a risk of SSIs (OR =1.72, 95% CI: 1.39–2.12, $I^2=0\%$; *Figure 5*).

Cigarette smoking

The data of 5 studies (15-17,21,25) reported a significant relationship between cigarette smoking and SSIs when comparing smoking and non-smoking patients (OR =1.35, 95% CI: 1.28–1.43, $I^2=0\%$; *Figure 6*).

Serum albumin

A meta-analysis of 3 studies (23,25,27) investigated the influence of serum albumin. The results showed that there was a high risk of SSIs when the serum albumin level of patients was over 2.5 g/dL (OR =3.36, 95% CI: 2.25–5.02, $I^2=0\%$; *Figure 7*).

Tumor location

Four studies (18,19,22,24) reported that tumor location was

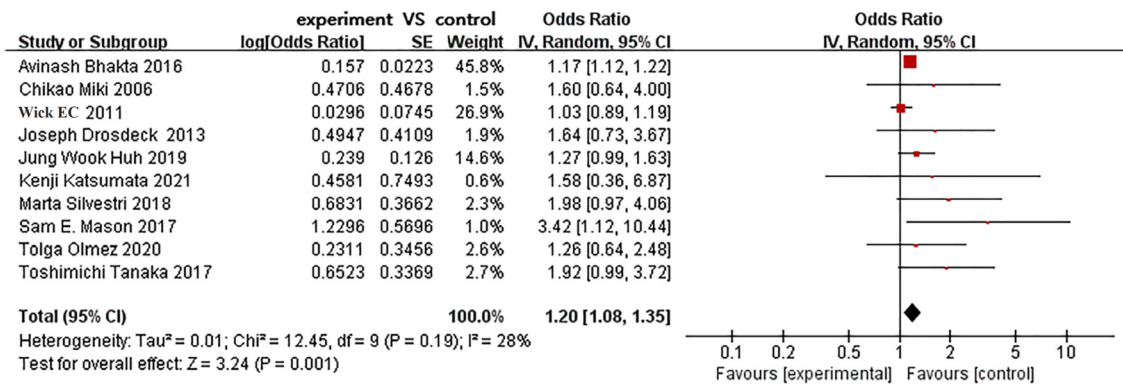


Figure 2 The forest plot showed the relationship between male gender and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

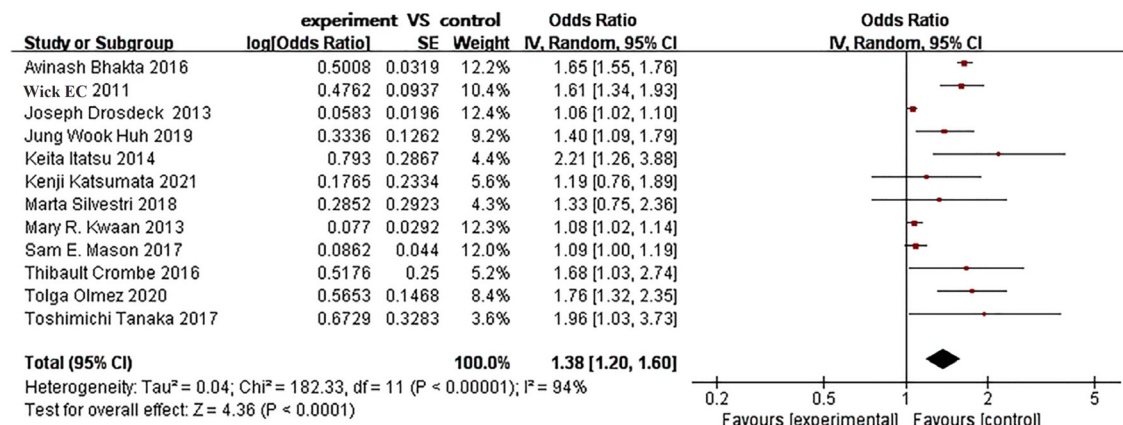


Figure 3 The forest plot showed the relationship between obesity and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

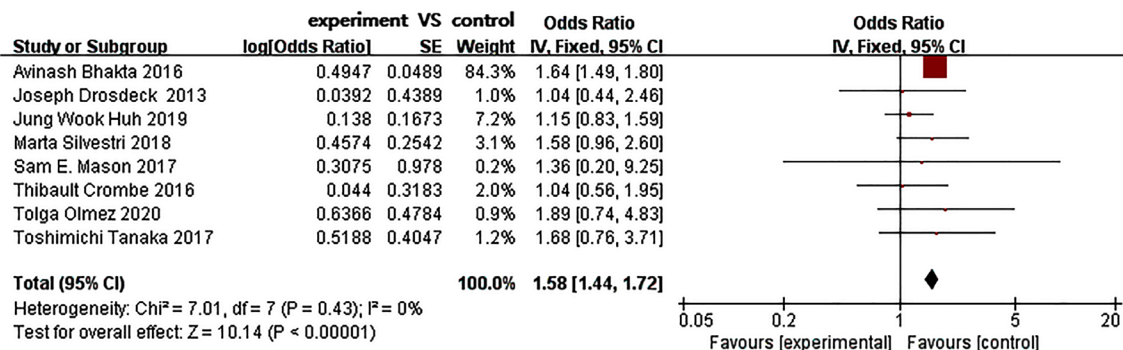


Figure 4 The forest plot showed the relationship between diabetes mellitus and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

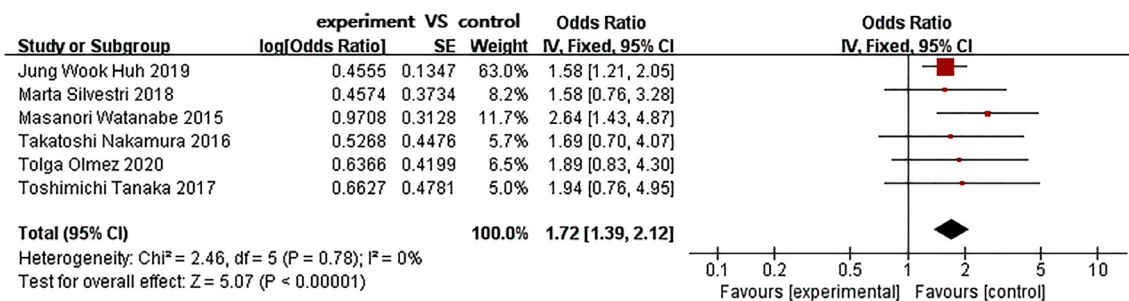


Figure 5 The forest plot showed the relationship between ASA score and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; ASA, American Society of Anaesthesiologists; SSI, surgical site infection.

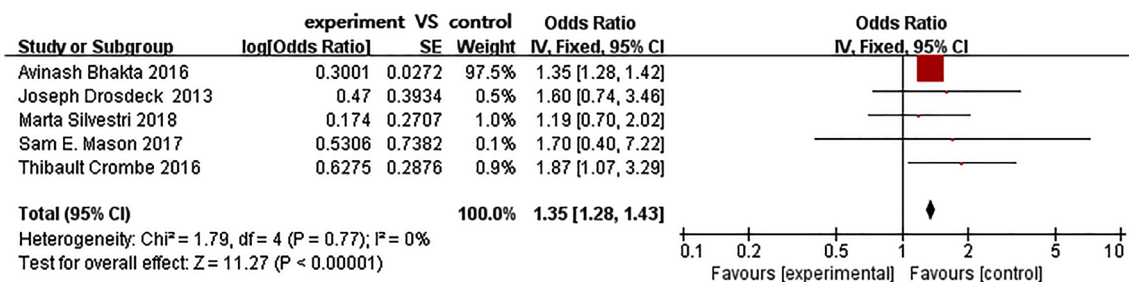


Figure 6 The forest plot showed the relationship between cigarette smoking and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

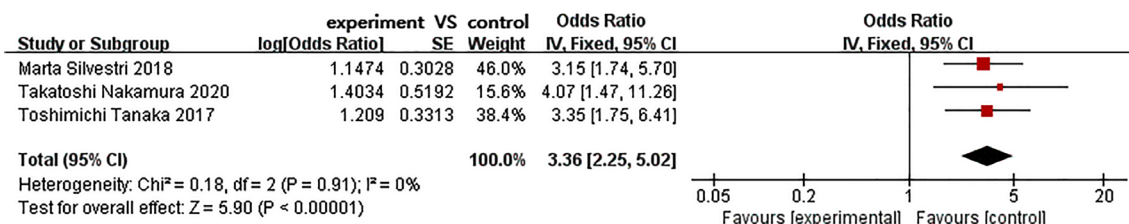


Figure 7 The forest plot showed the relationship between serum albumin and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

related to the risk of SSIs (OR =1.16, 95% CI: 0.72–1.86, I²=66%; Figure 8).

Age

Patient age was not directly related to SSI in colorectal cancer (OR =0.98, 95% CI: 0.93–1.03, I²=83%; Figure 9) in the included studies (15-19,21,24,25,27,29).

Treatment-related risk factors

Laparoscopic surgery

A meta-analysis of 3 studies (10,17,24) showed that patients who did not undergo selective laparoscopic colorectal cancer resection had a high incidence of SSIs (OR =1.75, 95% CI: 1.30–2.34, I²=42%; Figure 10).

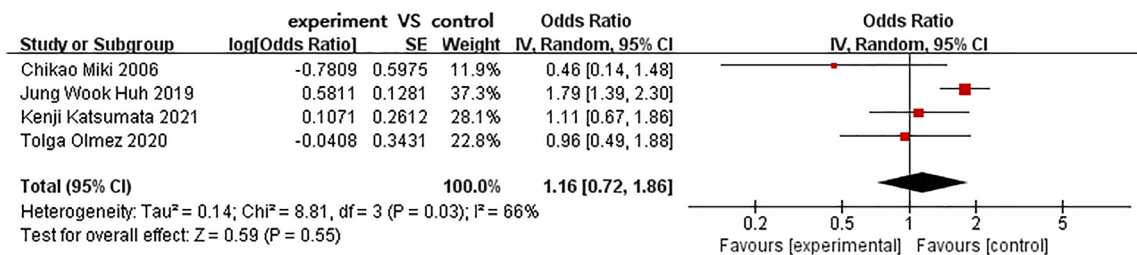


Figure 8 The forest plot showed the relationship between tumor location and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

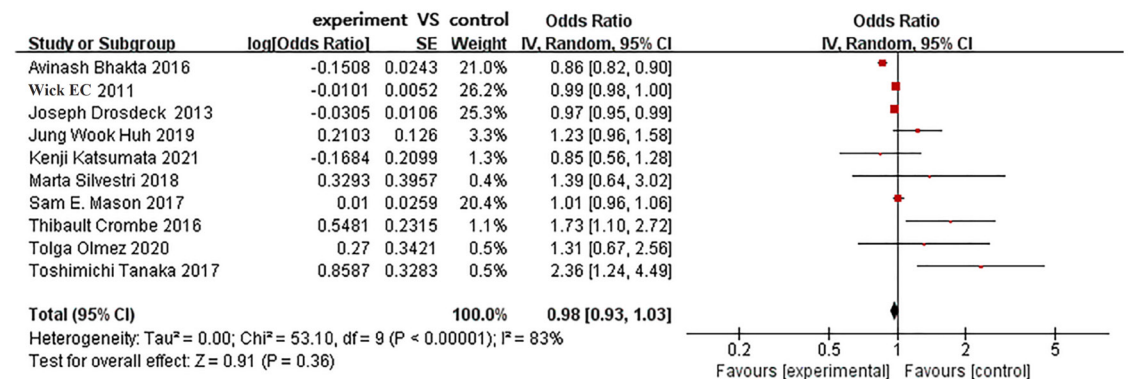


Figure 9 The forest plot showed the relationship between age and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

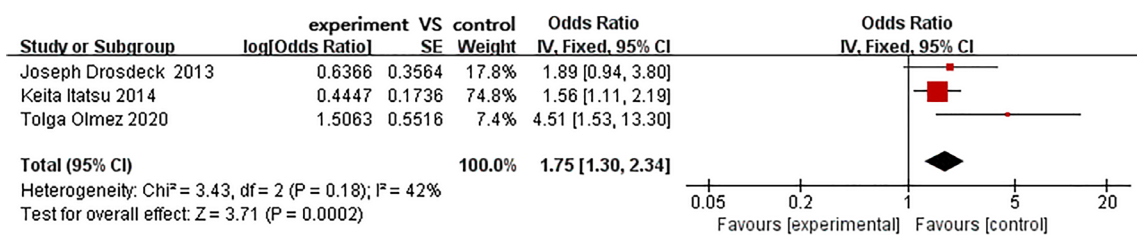


Figure 10 The forest plot showed the relationship between laparoscopic surgery and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

Operation time

Nine studies (15,16,18,19,21,24,25,27,29) reported that operation time could increase the risk of SSIs when the patient underwent a procedure longer than 180 minutes (OR =2.05, 95% CI: 1.61–2.59, I²=69%; Figure 11).

Blood transfusion

A meta-analysis of 4 studies (18,19,22,27) showed that

patients who received a perioperative blood transfusion had a higher risk of SSIs (OR =2.02, 95% CI: 1.48–2.77, I²=0%; Figure 12).

Blood loss

Three studies (22,24,27) reported that patients had an increased risk of SSIs when they experienced blood loss of at least 100 mL (OR =1.38, 95% CI: 0.72–2.66, I²=80%;

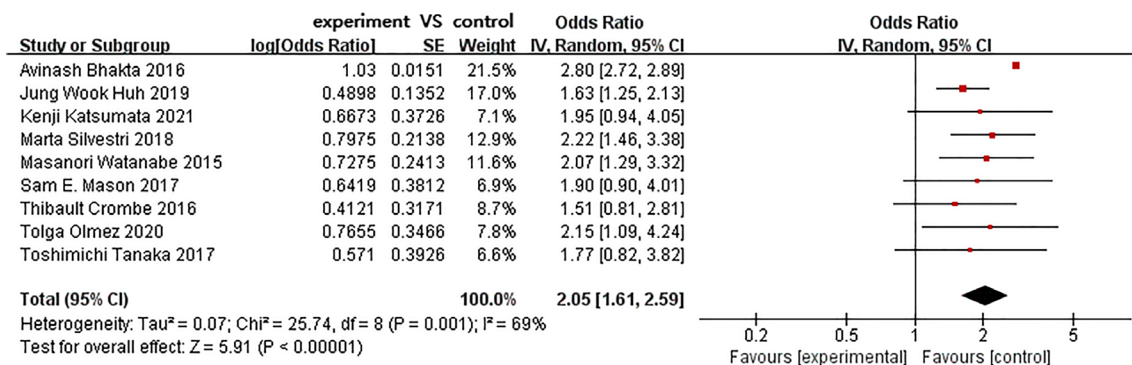


Figure 11 The forest plot showed the relationship between operation time and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

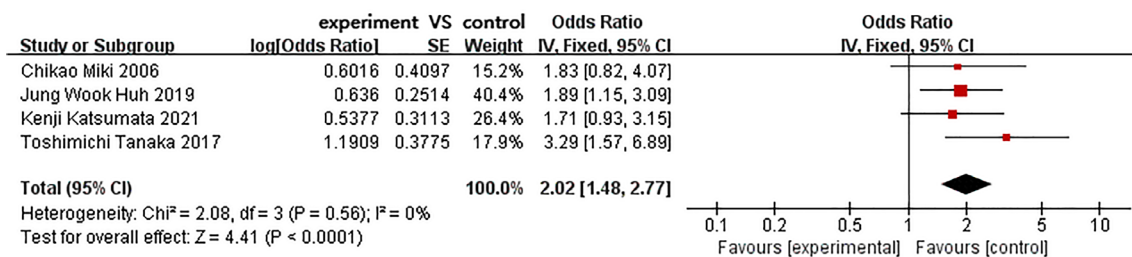


Figure 12 The forest plot showed the relationship between blood transfusion and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

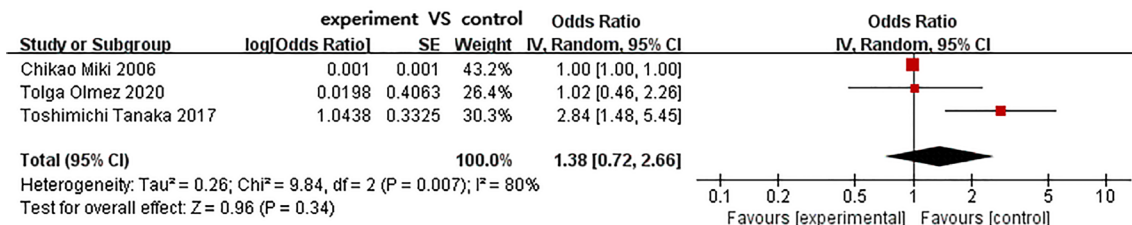


Figure 13 The forest plot showed the relationship between blood loss and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

Figure 13).

Abdominal surgical history

Three studies (16,17,28) reported abdominal surgical history. The results revealed that patients who had a history of abdominal surgery might have higher risk of SSIs (OR =1.64, 95% CI: 1.18–2.28, I²=0%; Figure 14).

Ostomy formation

A meta-analysis of 3 studies (24,25,27) showed that patients

with ostomy formation after colorectal cancer surgery had a lower incidence of SSIs (OR =0.74, 95% CI: 0.50–1.11, I²=0%; Figure 15).

Sensitivity analysis

We performed a sensitivity analysis to investigate heterogeneity in the included studies. The use of a fixed-effect model or a random-effects model did not significantly influence the merging direction of any risk factor (Table 4).

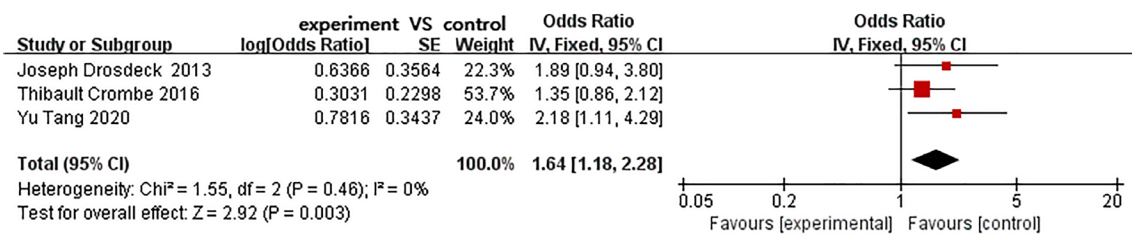


Figure 14 The forest plot showed the relationship between abdominal surgical history and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

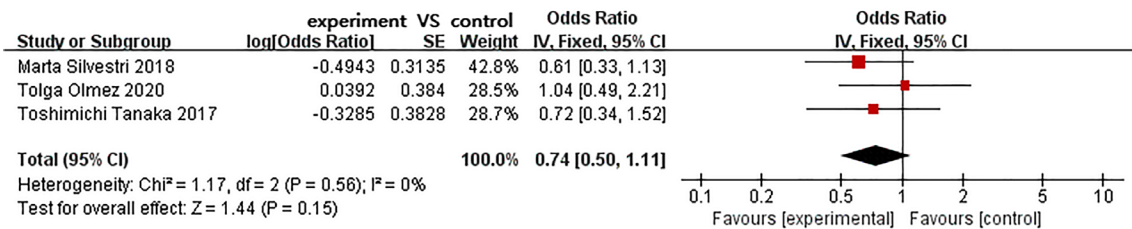


Figure 15 The forest plot showed the relationship between ostomy formation and the risk of SSI. 95% CI, 95% confidence interval; P value, probability value; IV, Inverse Variance methods; SE, standard error; SSI, surgical site infection.

Table 4 Sensitivity analysis of the meta-analysis

Risk factors	Fixed-effects model	Random-effects model
Male gender	1.17 (1.12, 1.22)	1.20 (1.08, 1.35)
Obesity	1.18 (1.15, 1.21)	1.38 (1.20, 1.60)
diabetes mellitus	1.58 (1.44, 1.72)	1.58 (1.44, 1.72)
ASA score	1.72 (1.39, 2.12)	1.72 (1.39, 2.12)
Laparoscopic surgery	1.75 (1.30, 2.34)	1.95 (1.20, 3.16)
Cigarette smoking	1.35 (1.28, 1.43)	1.35 (1.28, 1.43)
Operation time	2.77 (2.69, 2.85)	2.05 (1.61, 2.59)
Age	0.98 (0.97, 0.99)	0.98 (0.93, 1.03)
Blood loss	1.00 (1.00, 1.00)	1.38 (0.72, 2.66)
Blood transfusion	2.02 (1.48, 2.77)	2.02 (1.48, 2.77)
Tumor location	1.49 (1.20, 1.83)	1.16 (0.72, 1.86)
Serum albumin	3.36 (2.25, 5.02)	3.36 (2.25, 5.02)
Ostomy formation	0.74 (0.50, 1.11)	0.74 (0.50, 1.11)
Abdominal surgical history	1.64 (1.18, 2.28)	1.64 (1.18, 2.28)

Data was showed by OR (95% CI). ASA, American Society of Anesthesiologists; 95% CI, 95% confidence interval.

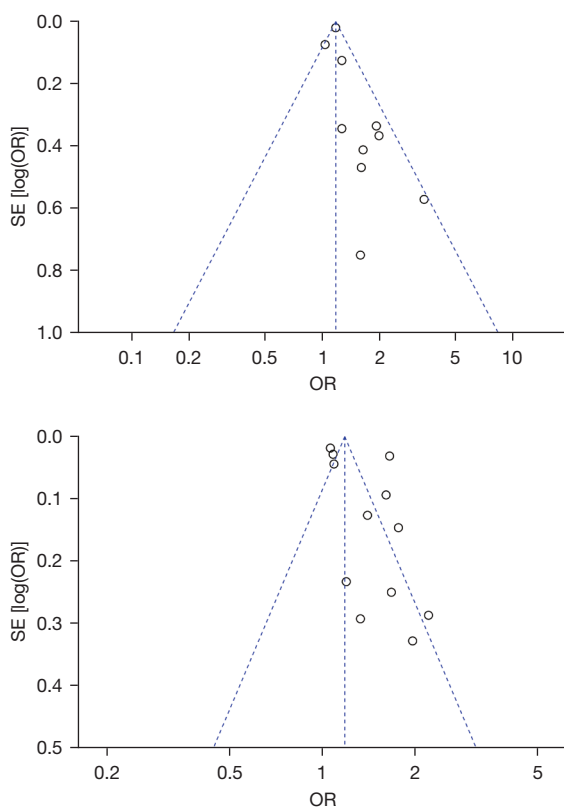


Figure 16 The funnel plot of male gender and obesity. OR, odds ratio; SE, standard error.

Therefore, the data reported in this meta-analysis may be regarded as stable.

Publication bias

Funnel plots of male gender and obesity were used to qualitatively evaluate publication bias (Figure 16). The plots showed that there was publication bias in some analyses. Therefore, the evidence related to these factors should be updated to eliminate potential publication bias.

Discussion

This meta-analysis investigated patient- and treatment-related risk factors of SSI. The results showed that male gender, obesity, diabetes mellitus, an ASA score of more than 3, cigarette smoking, a serum albumin level higher than 2.5 g/dL, tumor location, an operation time longer than 180 minutes, perioperative blood transfusion, blood loss of at least 100 mL, and abdominal surgical history

were important risk factors of SSI. However, laparoscopic colorectal cancer resection may be a protective factor against SSI. No heterogeneity between the included studies was found in the analyses of male gender, diabetes mellitus, ASA score, cigarette smoking, serum albumin level, blood transfusion, abdominal surgical history, laparoscopic colorectal cancer resection, or ostomy formation, which indicated that the results were stable.

Our results showed that male patients had a higher risk of SSI than female patients. This may be related to the different fat distribution between men and women (30). The surgical procedure could be more difficult for male patients who have excess visceral fat and abdominal obesity, which may lead to SSI.

Study has shown that obesity is a significant risk factor for SSI (30). In patients with obesity, the incision fat easily liquefies and forms a dead cavity, which delays wound healing and can result in SSI. Other factors contributing to the increased risk of postoperative SSI in obese patients with colorectal cancer include decreased antibiotic concentration in the tissues, decreased blood oxygen tension in the surgical wounds, antibacterial penetration damage in perioperative tissues, extended operation time, increased intra-operative bleeding, and decreased immune function (30).

Diabetes is a high-risk factor for postoperative infection in patients with colorectal cancer. Patients with diabetes have impaired glucose metabolism and glycolysis, which decreases the bactericidal function of neutrophils (31). In addition, the high sugar environment of wound effusion in patients with diabetes is more conducive to the growth and reproduction of bacteria. These factors increase the risk of infection in colorectal cancer patients with diabetes.

ASA score is an indicator of the physical condition of a patient before surgery. In our study, ASA score was related to the risk of SSI (32), and patients with a higher ASA score had a higher incidence of SSI (33). Blood transfusion was also a risk factor for SSI in our study (34). Therefore, improving the skills of surgeons could decrease the blood loss of patients during surgery, which may reduce the risk of SSI.

It has been reported that cigarette smoking can delay wound healing, which may lead to a risk of SSI. Our study found that patients who smoked had a higher risk of SSI in comparison with patients who did not smoke, which was consistent with the conclusions of the National Nosocomial Infections Surveillance System (NNIS) guidelines (35,36).

Clinical study (36) has confirmed that surgical duration

is a risk factor for SSI. The reasons for this are as follows: (I) the exposure of the surgical incision to air for a long time increases the chance of pathogen pollution; (II) the longer the operation time, the more complex the operation and the greater the trauma; and (III) prolonged anesthesia decreases immunity. Compared with traditional open surgery, laparoscopic surgery significantly reduces the exposure range of the incision, shortens the exposure time of abdominal organs to air, and decreases the opportunity for bacterial growth (37). This suggests that laparoscopic surgery could be a protective factor of SSI.

Surgery is an important means of diagnosis and treatment for patients with colorectal cancer, but the occurrence of SSI is inevitable due to many factors. This study aimed to reduce the incidence of infection by identifying patients who may be at a higher risk of developing SSI and provide recommendations to reduce these risks.

Conclusions

This study identified 12 risk factors for SSI in patients with colorectal cancer, including male gender, obesity, diabetes mellitus, an ASA score greater than 3, tumor location, cigarette smoking, a serum albumin level of more than 2.5 g/dL, laparoscopic surgery, an operation time longer than 180 minutes, blood transfusion, blood loss of at least 100 mL, and an abdominal surgical history of SSI. These risk factors may provide a scientific basis for the prevention of SSI in patients with colorectal cancer.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-627/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved.

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References

1. Kepler CK, Divi SN, Bronson WH, et al. General Principles in the Consensus of SSI Management After Spine Surgery. *Clin Spine Surg* 2020;33:E191-8.
2. Singh SK. Superglue slide impression (SSI) method: a novel diagnostic application for canine demodicosis. *Exp Appl Acarol* 2019;79:387-93.
3. O'Donnell RL, Angelopoulos G, Beirne JP, et al. Impact of surgical site infection (SSI) following gynaecological cancer surgery in the UK: a trainee-led multicentre audit and service evaluation. *BMJ Open* 2019;9:e024853.
4. Gaynes RP, Culver DH, Horan TC, et al. Surgical site infection (SSI) rates in the United States, 1992-1998: the National Nosocomial Infections Surveillance System basic SSI risk index. *Clin Infect Dis* 2001;33 Suppl 2:S69-77.
5. Lietard C, Thébaud V, Besson G, et al. Surveillance for surgical site infection (SSI) after neurosurgery: influence of the US or Brest (France) National Nosocomial Infection Surveillance risk index on SSI rates. *Infect Control Hosp Epidemiol* 2008;29:1084-7.
6. Percario R, Panaccio P, di Mola FF, et al. The Complex Network between Inflammation and Colorectal Cancer: A Systematic Review of the Literature. *Cancers (Basel)* 2021;13:6237.
7. Zhang Y, Chen Z, Li J. The current status of treatment for colorectal cancer in China: A systematic review. *Medicine (Baltimore)* 2017;96:e8242.
8. Kamboj M, Childers T, Sugalski J, et al. Risk of Surgical Site Infection (SSI) following Colorectal Resection Is Higher in Patients With Disseminated Cancer: An NCCN Member Cohort Study. *Infect Control Hosp Epidemiol* 2018;39:555-62.
9. Sagawa M, Yokomizo H, Yoshimatsu K, et al. Relationship between Surgical Site Infection (SSI) Incidence and Prognosis in Colorectal Cancer Surgery. *Gan To Kagaku*

- Ryoho 2017;44:921-3.
10. Itatsu K, Sugawara G, Kaneoka Y, et al. Risk factors for incisional surgical site infections in elective surgery for colorectal cancer: focus on intraoperative meticulous wound management. *Surg Today* 2014;44:1242-52.
 11. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008-12.
 12. Cheng H, Clymer JW, Po-Han Chen B, et al. Prolonged operative duration is associated with complications: a systematic review and meta-analysis. *J Surg Res* 2018;229:134-44.
 13. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603-5.
 14. Nakamura T, Takayama Y, Sato T, et al. Risk Factors for Wound Infection After Laparoscopic Surgery for Colon Cancer. *Surg Laparosc Endosc Percutan Tech* 2020;30:45-8.
 15. Bhakta A, Tafen M, Glotzer O, et al. Increased Incidence of Surgical Site Infection in IBD Patients. *Dis Colon Rectum* 2016;59:316-22.
 16. Crombe T, Bot J, Messenger M, et al. Malignancy is a risk factor for postoperative infectious complications after elective colorectal resection. *Int J Colorectal Dis* 2016;31:885-94.
 17. Drosdeck J, Harzman A, Suzo A, et al. Multivariate analysis of risk factors for surgical site infection after laparoscopic colorectal surgery. *Surg Endosc* 2013;27:4574-80.
 18. Huh JW, Lee WY, Park YA, et al. Oncological outcome of surgical site infection after colorectal cancer surgery. *Int J Colorectal Dis* 2019;34:277-83.
 19. Katsumata K, Enomoto M, Ishizaki T, et al. Risk factors for surgical site infection and association of surgical site infection with survival of lower rectal cancer patients without clinical lateral pelvic lymph node metastasis (clinical Stage II/III): Analysis of data from JCOG0212. *Clin Exp Metastasis* 2021;38:459-66.
 20. Kwaan MR, Sirany AM, Rothenberger DA, et al. Abdominal wall thickness: is it associated with superficial and deep incisional surgical site infection after colorectal surgery? *Surg Infect (Larchmt)* 2013;14:363-8.
 21. Mason SE, Kinross JM, Hendricks J, et al. Postoperative hypothermia and surgical site infection following peritoneal insufflation with warm, humidified carbon dioxide during laparoscopic colorectal surgery: a cohort study with cost-effectiveness analysis. *Surg Endosc* 2017;31:1923-9.
 22. Miki C, Inoue Y, Mohri Y, et al. Site-specific patterns of surgical site infections and their early indicators after elective colorectal cancer surgery. *Dis Colon Rectum* 2006;49:S45-52.
 23. Nakamura T, Sato T, Takayama Y, et al. Risk Factors for Surgical Site Infection after Laparoscopic Surgery for Colon Cancer. *Surg Infect (Larchmt)* 2016;17:454-8.
 24. Olmez T, Karakose E, Keklikkiran ZZ, et al. Relationship between Sarcopenia and Surgical Site Infection in Patients Undergoing Colorectal Cancer Surgical Procedures. *Surg Infect (Larchmt)* 2020;21:451-6.
 25. Silvestri M, Dobrinja C, Scomersi S, et al. Modifiable and non-modifiable risk factors for surgical site infection after colorectal surgery: a single-center experience. *Surg Today* 2018;48:338-45.
 26. Wick EC, Hirose K, Shore AD, et al. Surgical site infections and cost in obese patients undergoing colorectal surgery. *Arch Surg* 2011;146:1068-72.
 27. Tanaka T, Sato T, Yamashita K, et al. Effect of Preoperative Nutritional Status on Surgical Site Infection in Colorectal Cancer Resection. *Dig Surg* 2017;34:68-77.
 28. Tang Y, Zhang R, Yang W, et al. Prognostic Value of Surgical Site Infection in Patients After Radical Colorectal Cancer Resection. *Med Sci Monit* 2020;26:e928054.
 29. Watanabe M, Suzuki H, Nomura S, et al. Performance assessment of the risk index category for surgical site infection after colorectal surgery. *Surg Infect (Larchmt)* 2015;16:84-9.
 30. Fujii T, Tabe Y, Yajima R, et al. Effects of subcutaneous drain for the prevention of incisional SSI in high-risk patients undergoing colorectal surgery. *Int J Colorectal Dis* 2011;26:1151-5.
 31. Webb MA, Bleszynski MS, Chen L, et al. Incisional wound VAC and risk-adjusted SSI rates in colorectal surgery: A tertiary centre experience. *Am J Surg* 2019;217:948-53.
 32. Sathiyakumar V, Molina CS, Thakore RV, et al. ASA score as a predictor of 30-day perioperative readmission in patients with orthopaedic trauma injuries: an NSQIP analysis. *J Orthop Trauma* 2015;29:e127-32.
 33. Xu Z, Qu H, Kanani G, et al. Update on risk factors of surgical site infection in colorectal cancer: a systematic review and meta-analysis. *Int J Colorectal Dis* 2020;35:2147-56.
 34. Kim T, Purdy MP, Kendall-Rauchfuss L, et al. Myomectomy associated blood transfusion risk and morbidity after surgery. *Fertil Steril* 2020;114:175-84.
 35. Konishi T, Watanabe T, Kishimoto J, et al. Elective

- colon and rectal surgery differ in risk factors for wound infection: results of prospective surveillance. *Ann Surg* 2006;244:758-63.
36. Xu Z, Qu H, Gong Z, et al. Risk factors for surgical site infection in patients undergoing colorectal surgery: A meta-analysis of observational studies. *PLoS One* 2021;16:e0259107.
37. Baixauli J, Cienfuegos JA, Martinez Regueira F, et al. Conversion to Open Surgery in Laparoscopic Colorectal Cancer Resection: Predictive Factors and its Impact on Long-Term Outcomes. A Case Series Study. *Surg Laparosc Endosc Percutan Tech* 2021;32:28-34.

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