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The impact of diabetes on postoperative infections in colorectal cancer: A meta-analysis

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Abstract. Objective: This study aims to analyze and summarize the evidence concerning the relationship between diabetes and postoperative infections in colon cancer through a literature review. Methods: A comprehensive search was conducted on Chinese databases, including CNKI, VIP, Wanfang, and the biomedical literature database, as well as the English database PubMed. The search covered the period from February 1, 2003, to February 28, 2023. The Newcastle-Ottawa Scale was employed to score the included literature, and funnel plots along with Egger's regression test were used to analyze publication bias. Stata 12.0 was utilized for the analysis of the collected raw data. Results: Following inclusion and exclusion criteria, this study incorporated seven retrospective studies, with a total of 4607 cases in the infection group and 9102 cases in the non-infection group. The quality scores of the seven studies ranged between 7 and 8 points. Funnel plot and Egger's regression test analyses revealed no significant publication bias in the included literature. A correlation was identified between diabetes and postoperative infections in colon cancer, implicating diabetes as a risk factor for such infections. Subgroup analysis indicated that nationality, surgical methods, and infection types had no significant impact on the meta-analysis results. Conclusion: The analysis revealed a significant correlation between diabetes and postoperative infections in colon cancer. Diabetes emerged as a risk factor for postoperative infections, with odds ratios (OR) of 3.82 ($P>0.1$) and 95% CI of 2.91-5.01. Controlling blood glucose levels was associated with a reduced risk of postoperative infections in colon cancer.

Keywords: Diabetes; Colorectal Cancer; Postoperative Infection; Meta-Analysis

1. Introduction

Colorectal cancer is the most common malignant tumor in the gastrointestinal tract. According to data from the International Agency for Research on Cancer (IARC), a subsidiary of the World Health Organization, approximately 1.36 million new cases of colorectal cancer were reported worldwide in 2012, ranking it as the third most common malignancy [1]. Surgery stands as the primary treatment for colorectal cancer, and studies have indicated that the 5-year survival rate for early-stage colorectal cancer patients undergoing surgery is over 90% [2]. Despite the evident clinical success of surgery, postoperative complications significantly impact patient prognosis and survival. The incidence of

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postoperative infectious complications is on the rise [3], profoundly affecting both the quality of surgery and the postoperative recovery outcomes for patients [4, 5]. Therefore, understanding and prioritizing the risk factors for postoperative infections is crucial to effectively prevent their occurrence. This study aims to further investigate the correlation between postoperative infections in colorectal cancer patients and a history of diabetes. The goal is to clarify the risk factors influencing postoperative infections in colorectal cancer, providing a scientific basis for the effective prevention of postoperative infections.

2. Research Methods

2.1. Search Methods

A systematic search was conducted in foreign language databases, including PubMed, and Chinese databases, including CNKI, VIP, Wanfang Data, and CBM. Keywords used for the foreign language databases included cancer of colon, carcinoma of colon, colon cancer; Surgical treatment, Operative treatment, operative therapy; postoperative colorectal cancer, postoperative colon cancer; diabetes mellitus, diabetes. Keywords used for the Chinese databases included colon cancer, colorectal cancer, surgery, postoperative infection, diabetes. The search period ranged from February 1, 2003, to February 28, 2023.

2.2. Inclusion and Exclusion Criteria

2.2.1. Inclusion Criteria. 1. The research subjects had a confirmed diagnosis of colon cancer [6]. 2. The study included various research types, such as randomized controlled trials, cohort studies, case-control studies, retrospective studies, prospective studies, etc., with available research data. 3. The research subjects underwent surgical treatment, including laparoscopic and open surgeries, radical procedures, and resections. 4. The research subjects experienced postoperative infections and met the diagnostic criteria for postoperative infections [7]. 5. The study results provided or could be converted into OR values, RR values, and 95% CIs.

2.2.2. Exclusion Criteria. 1. The research subjects did not meet the diagnosis of colon cancer. 2. The literature lacked specific research data or had incomplete data. 3. The research subjects had infections before surgery. 4. Duplicate publications. 5. Review articles, nursing-related studies, meta-analyses, and similar literature.

2.3. Literature Screening, Data Extraction, and Quality Assessment

Unrelated literature was filtered out by reading the titles, and two researchers independently extracted the characteristics of included studies (including authors, publication years, total number of participants, study countries, numbers of patients with and without diseases, etc.). The Newcastle-Ottawa Quality Assessment Scale (NOS) was used for quality assessment of the included literature [8, 9].

2.4. Statistical Methods

Stata 12.0 was used for data analysis. When $P > 0.1$, $I^2 \leq 30\%$ indicated low heterogeneity between studies, $30\% < I^2 \leq 50\%$ indicated moderate heterogeneity, and $I^2 > 50\%$ indicated high heterogeneity. For low and moderate heterogeneity, a fixed-effects model was used; for high heterogeneity, a random-effects model was adopted [8, 9]. Funnel plots and Egger's test were used to analyze publication bias.

3. Results

3.1. Literature Search Results

Through the preliminary screening of databases, a total of 3081 Chinese and 2003 English articles were obtained. After excluding irrelevant literature based on titles and reading abstracts, 4979 articles were eliminated. A total of 105 articles were initially included after the preliminary screening. Following the

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inclusion and exclusion criteria, and after reading the full texts, 96 articles were further excluded, leaving 9 articles. Using the NOS quality assessment score, literature with a score ≥7 points was included, resulting in a final inclusion of 7 qualified articles [10-16]. The specific flowchart is shown in Figure 1.

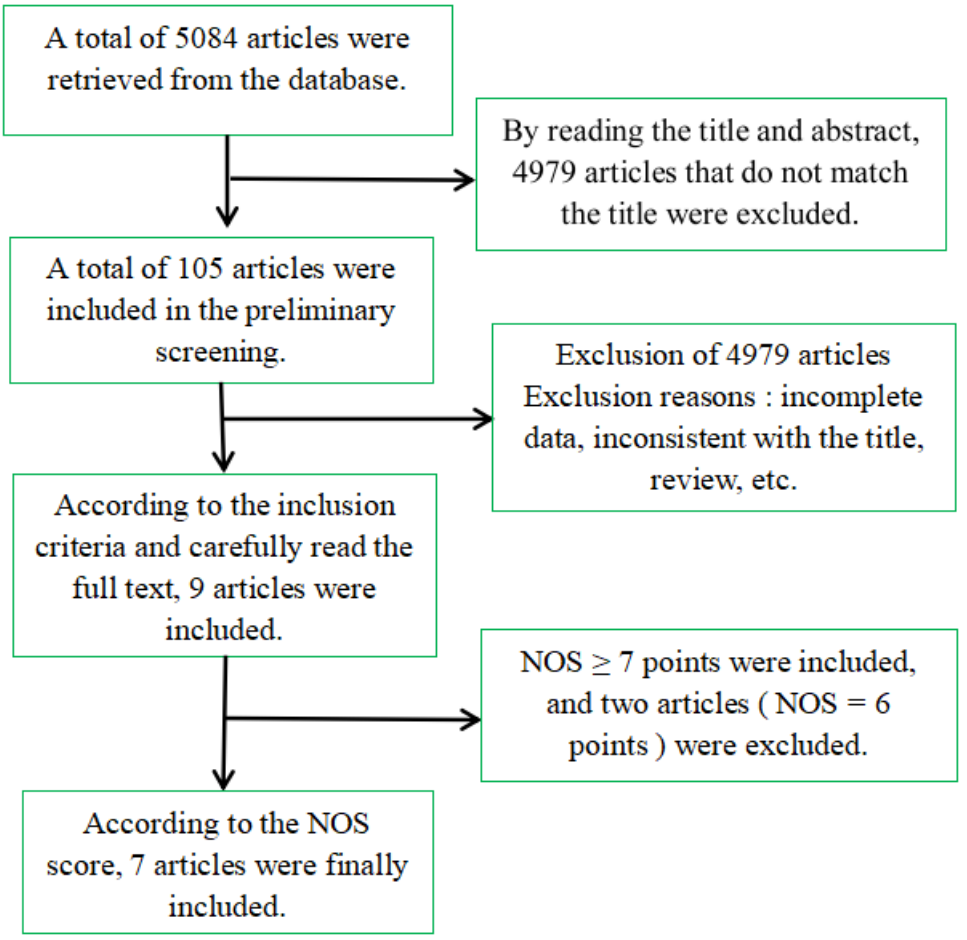

Figure 1. Flowchart

3.2. Basic Characteristics of Included Literature

Among the 7 included articles, 5 were in Chinese and 2 were in English, all of which were retrospective studies published between 2009 and 2021. The total sample size for the infection group was 271, and for the non-infection group, it was 3503. See Table 1.

Table 1. Basic Characteristics of Included Literature

Author	Publication Year	Region	Age	Infection Group (n)	Non-Infection Group (n)	NOS Score
Takatosh Nakamura [10]	2016	Japan	26–91	27 (7)	643 (68)	8
Wang Haohua [11]	2021	China	28–75	63 (34)	321 (78)	7
Du Jianjun [12]	2019	China	27–70	61 (33)	320 (79)	7

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Table 1. (continued)

Shi Chenlei [13]	2009	China	44–82	29 (16)	1028 (116)	7
Zhang Honglai [14]	2017	China	20–86	15 (4)	360 (42)	7
Lei Jin [15]	2019	China	21–86	20 (5)	466 (25)	7
Liu Peichang [16]	2019	China	47–70	56 (21)	365 (62)	7

Note: *n* represents the number of diabetic patients.

3.3. Meta-Analysis Results

3.3.1. Meta-Analysis of the Impact of Diabetes on Postoperative Infections in Colorectal Cancer. The relationship between diabetes and postoperative infections in colorectal cancer is illustrated in Figure 2. The heterogeneity test among studies indicated I^2 = 23.0% (P > 0.1), suggesting low heterogeneity among the studies, and a fixed-effects model was applied. The meta-analysis results reveal that diabetes is a risk factor for postoperative infections in colorectal cancer, with an odds ratio (OR) of 3.82 (P > 0.1) and a 95% confidence interval (CI) of 2.91-5.01.

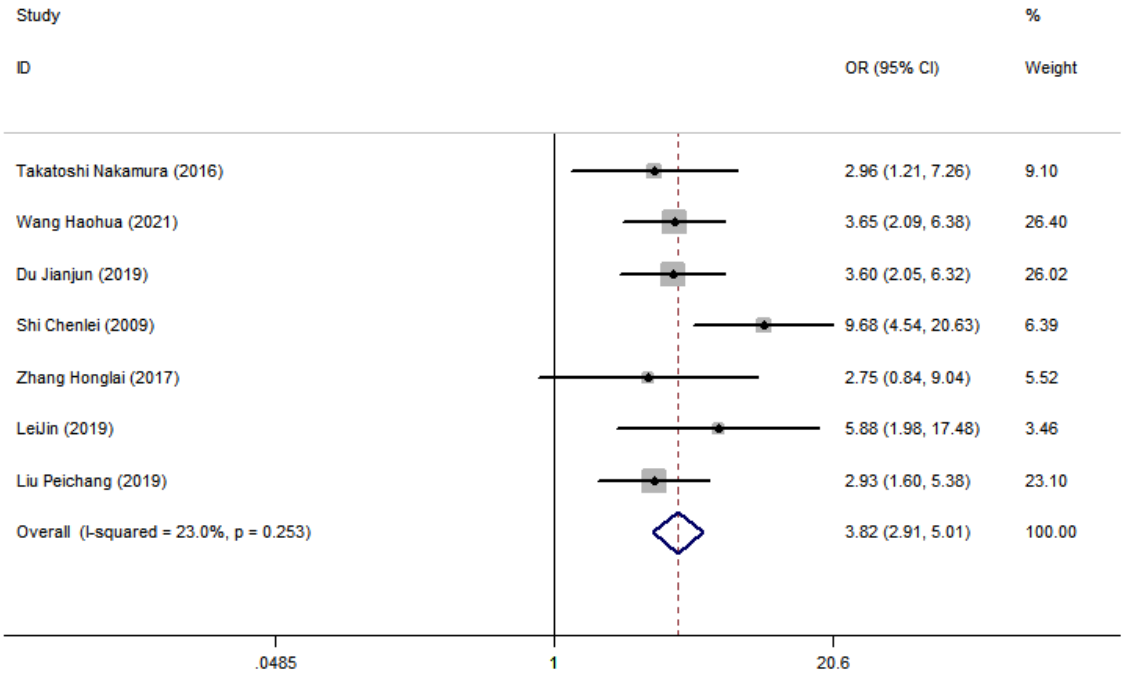

Figure 2. Forest Plot of the Impact of Diabetes on Postoperative Infections in Colorectal Cancer

3.3.2. Sensitivity Analysis. Sensitivity analysis was conducted using the one-by-one exclusion method to observe the combined results, as depicted in Figure 3. The forest plot shows that even after excluding the majority of the literature, the combined results for the remaining studies still maintain a 95% confidence interval of 2.91-5.01. This indicates the overall stability of the combined results in this study.

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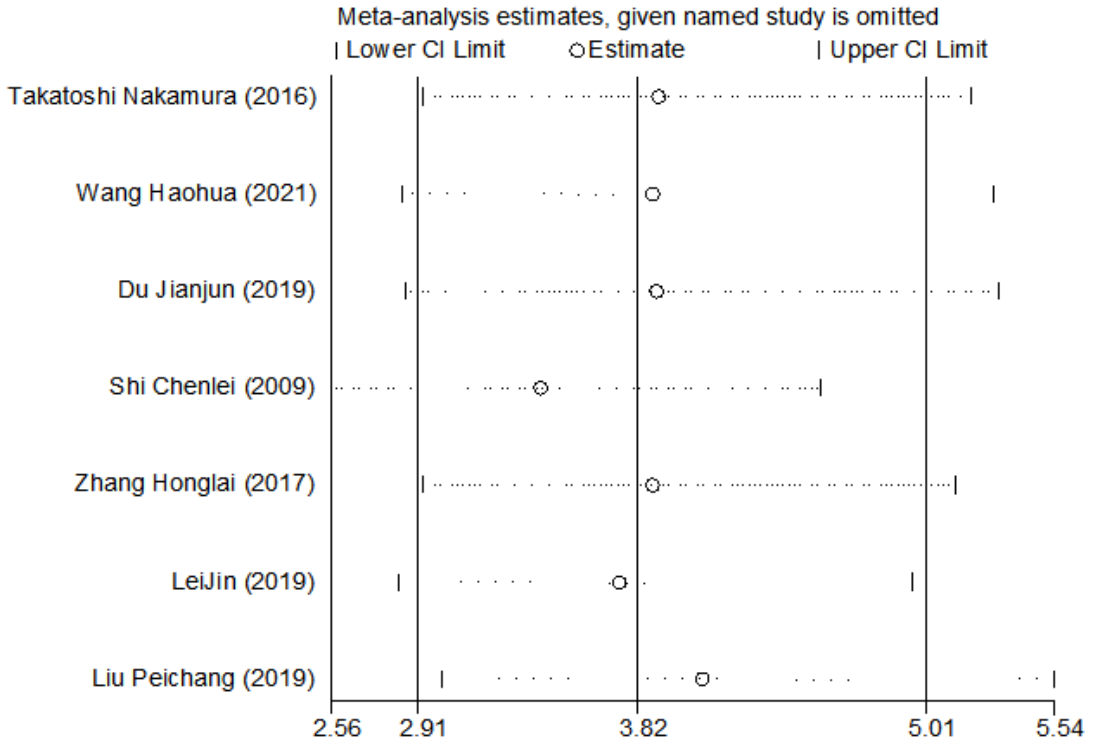

Figure 3. Sensitivity Analysis

3.3.3. Publication Bias Analysis. A funnel plot was employed to examine publication bias, as shown in Figure 4. Further examination using Egger's test yielded a result of P =0.707 (P > 0.05), indicating no significant publication bias, as detailed in Figure 5.

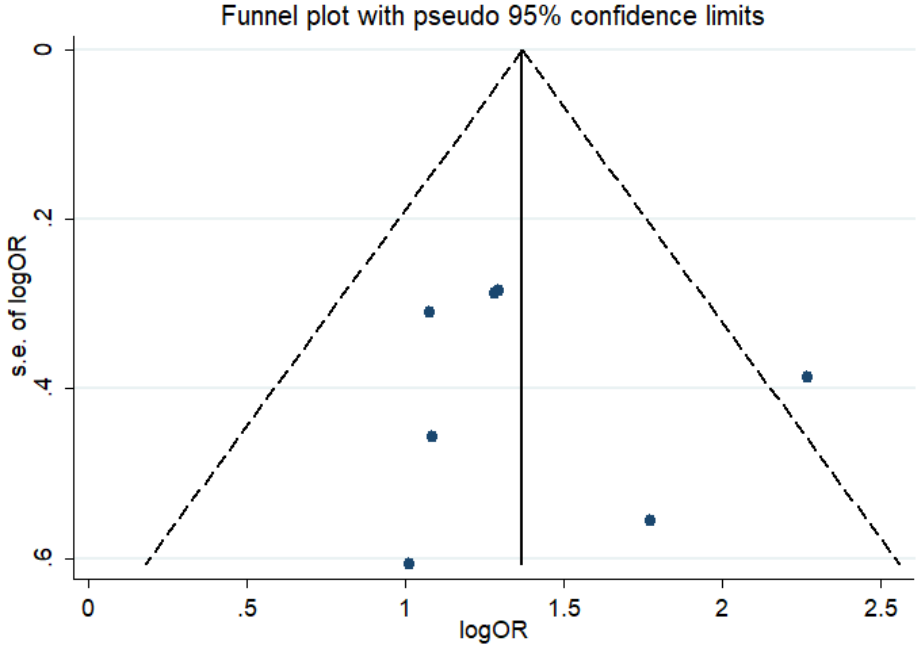

Figure 4. Funnel Plot of Publication Bias Risk

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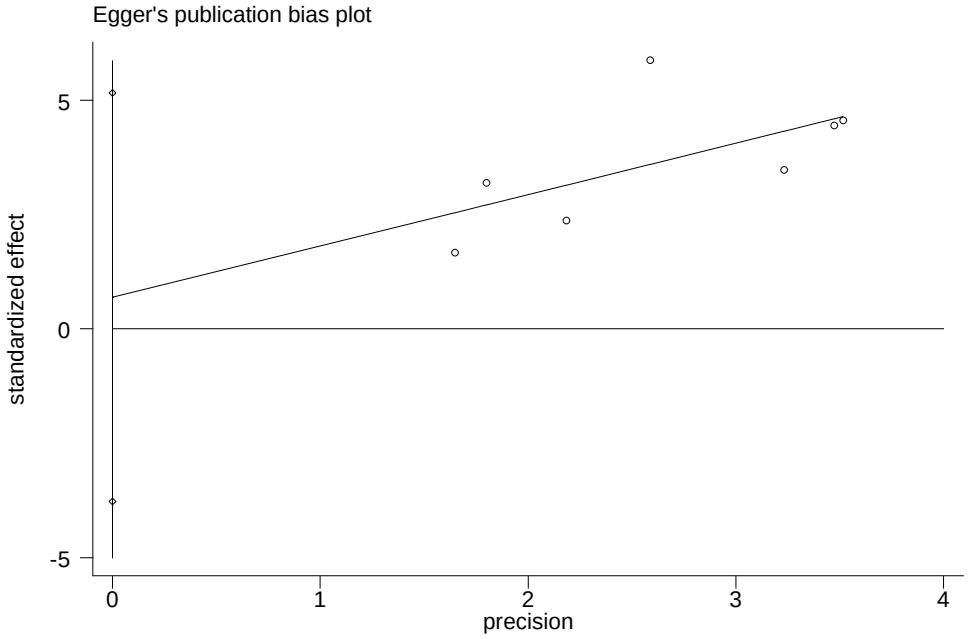

Figure 5. Egger's Test

3.3.4. Subgroup Analysis. Subgroup analyses were conducted based on the country, surgical method, and type of infection to investigate whether these factors significantly influenced the results. Subgroup analyses for country, surgical method, and type of infection all resulted in $I^2 < 50\%$, $P > 0.1$, demonstrating no statistical heterogeneity, as illustrated in Figure 6, Figure 7, and Figure 8. This indicates that the grouping factors of country, surgical method, and type of infection have no significant impact on the meta-analysis.

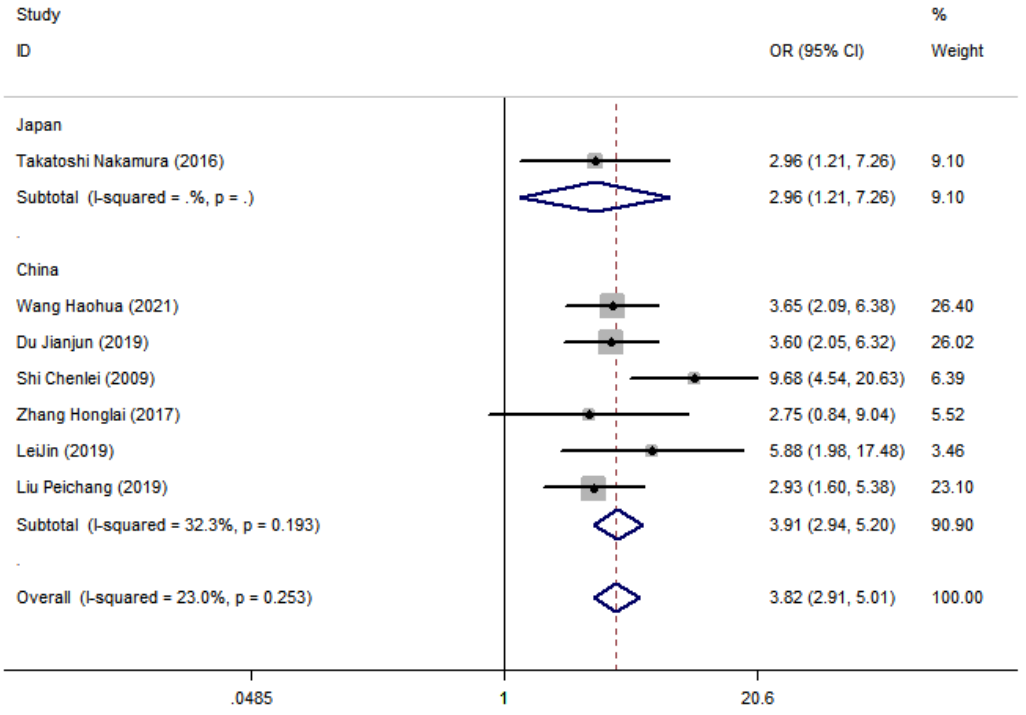

Figure 6. Subgroup Analysis by Country

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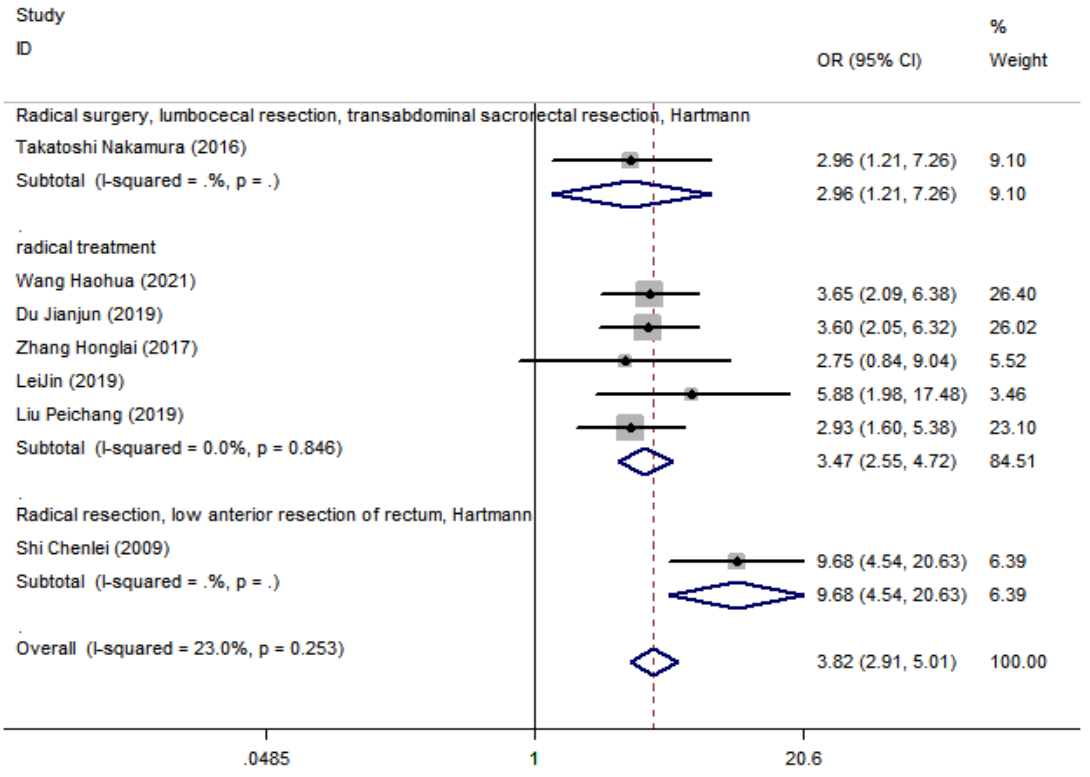

Figure 7. Subgroup Analysis by Surgical Method

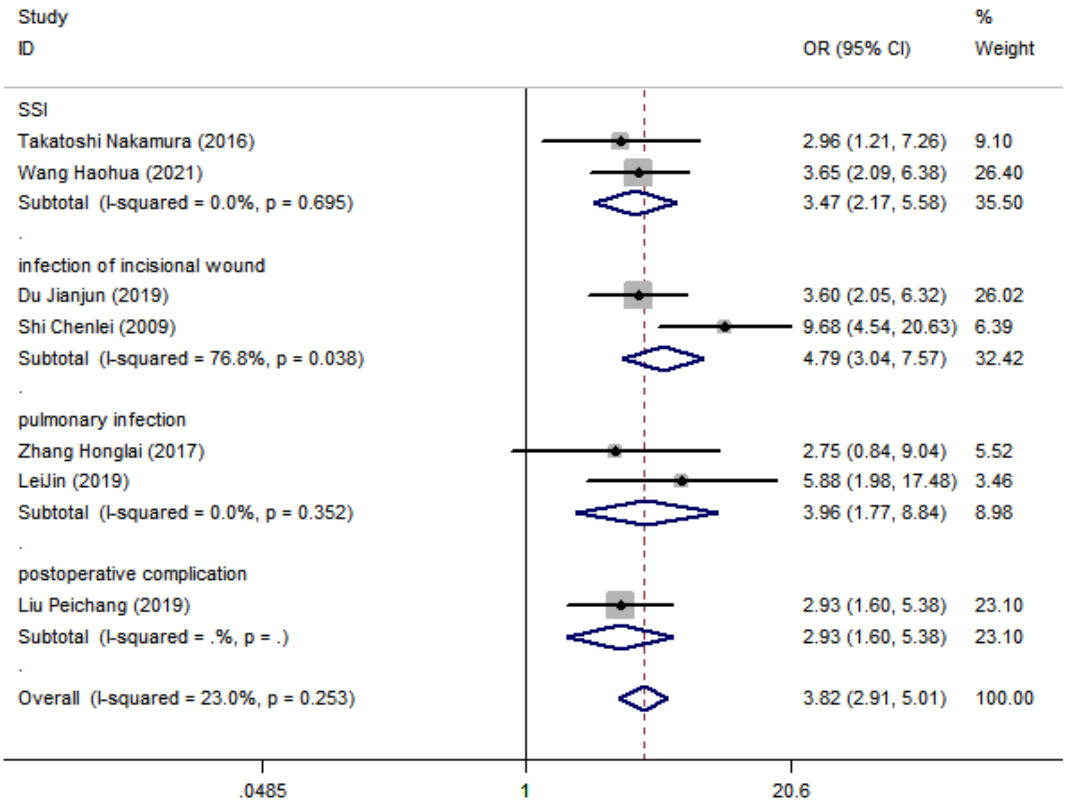

Figure 8. Subgroup Analysis by Type of Infection

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4. Discussion

In recent years, with social development, changes in dietary habits, and lifestyle alterations, the incidence rates of diabetes and colorectal cancer have gradually increased. The prevalence of diabetes in colorectal cancer patients is on the rise. The postoperative infection rate in colorectal cancer patients can reach 3% to 26% [17, 18], and postoperative infections in colorectal cancer can induce a systemic inflammatory response syndrome, leading to sepsis and death in severe cases.

The proactive and effective reduction of postoperative infections in colorectal cancer patients has garnered significant attention from medical professionals. Various measures have been implemented, such as strengthening rehabilitation treatment, employing infection prevention strategies [19-21], and utilizing preoperative mechanical bowel preparation combined with oral antibiotics [22-25]. Gao Jiali [26] demonstrated the significant advantages of Vacuum Assisted Closure (VAC) treatment in the case of a patient with postoperative infection and wound dehiscence following surgery for sigmoid colon cancer. Shigetomi et al. [27] provided evidence that Negative Pressure Wound Therapy with Instillation and a Dressing (NPWTi-d) may play a crucial role in wound dehiscence with postoperative infection in colorectal cancer patients, as evidenced by the formation of benign granulation tissue on the small intestine on the 25th postoperative day. It is evident that timely and effective measures are crucial for the prognosis and outcome of the disease [28]. Studies [29] suggest that predicting postoperative infections in colorectal cancer patients with diabetes can be done with high accuracy through PGSGA scoring, soluble triggering receptor expressed on myeloid cells 1 (sTREM-1), C-reactive protein (CRP), and vascular endothelial growth factor (VEGF). Therefore, interventions for colorectal cancer patients with diabetes, such as preoperative assessments, effective blood sugar level control, adequate preoperative preparation, and antibiotic application, are of paramount significance. These measures contribute significantly to improving surgical quality, facilitating early patient recovery, and ensuring substantial benefits for the patients.

5. Conclusion

Numerous studies have explored the risk factors for colorectal cancer and the risk factors for postoperative infections in colorectal cancer patients, particularly focusing on the association between diabetes and colorectal cancer. The results of these studies consistently indicate that diabetes is a risk factor for both colorectal cancer and postoperative infections. In this study, the odds ratio (OR) was found to be 3.82, with a 95% confidence interval (CI) of 2.91-5.01, providing evidence that diabetes is indeed a risk factor for postoperative infections in colorectal cancer patients. The sensitivity analysis confirmed the stability of the combined results, with a 95% CI of 2.91-5.01. Furthermore, subgroup analyses based on country, surgical method, and infection type demonstrated no significant heterogeneity, with $I^2 < 50\%$ and $P > 0.1$, suggesting that postoperative infections in colorectal cancer are not influenced by factors such as country and surgical approach. This aligns with findings in relevant literature both domestically and internationally. Patients with diabetes experience a reduced resistance to pathogens, leading to a significantly higher incidence of postoperative infections compared to non-diabetic patients [30, 31]. This may be attributed to the prolonged state of disrupted sugar metabolism and decreased sugar fermentation levels in diabetic patients, resulting in compromised immune function [32, 33]. The hyperglycemic environment favors rapid proliferation of pathogenic bacteria in the abdominal cavity, triggering postoperative infections [34]. Studies [35] indicate that diabetes induces platelet-endothelial cell adhesion molecule-1 (PECAM-1) defects and/or internalization in the tumor microenvironment, promoting the release of β-catenin from cell membranes. Activation of the Akt/GSK-3β signaling pathway inhibits the degradation of β-catenin, leading to its accumulation in the cytoplasm and translocation to the cell nucleus, ultimately inducing endothelial-mesenchymal transition and accelerating the progression of colorectal cancer combined with diabetes. In summary, postoperative infections in colorectal cancer patients are associated with factors such as high glucose levels, metabolic disorders, weakened immune function, oxidative stress, inflammatory responses, and epigenetic inheritance. Insulin/IGF signaling, dysbiosis of the intestinal microbiota, and other factors may also be involved, collectively activating and enhancing the expression of signaling pathways such as WNT/β-

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catenin, ERK1/2 and JNK MAPK, JAK2-STAT3, and MAPK in tumor cells, thereby increasing the proliferation, survival, invasion, and migration capabilities of tumor cells [36]. These mechanisms may directly or indirectly contribute to the rapid progression of the disease. Therefore, gaining a deeper understanding of the risk or influencing factors of colorectal cancer in patients with diabetes and studying its mechanisms can aid in reasonable prevention, timely intervention, and effective treatment of the disease.

Limitations and prospects of this study: (1) Some relevant studies both domestically and internationally have reported on other factors influencing postoperative infections in colorectal cancer patients through Meta-analysis. Due to the type of literature or other reasons, these could not be included in this Meta-analysis, affecting the quality and results of the analysis; (2) The foreign language database in this study only included PubMed, resulting in only two English-language articles, potentially causing bias in this Meta-analysis and impacting the results; (3) The research types included in the literature of this study are all retrospective studies, which have limitations. Therefore, a large number of prospective, multicenter clinical studies are needed to verify the results; (4) Clinically, comprehensive preoperative assessments should be conducted for colorectal cancer patients with diabetes scheduled for surgery, monitoring blood sugar fluctuations during three meals, and timely controlling blood sugar levels. In the future, clinical application of relevant predictive models for comprehensive risk assessment and related testing screening for patients is anticipated, aiming to reduce the incidence and mortality of postoperative infections in colorectal cancer patients with diabetes. In addition, in-depth research on the mechanisms by which diabetes promotes colorectal cancer development is needed, leading to the development of new treatment drugs and strategies with the goal of improving patient survival rates.

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