Meta-analysis of risk factors for postoperative pulmonary infection in patients with colorectal cancer after radiotherapy

Z. Xiaoshuai^{1#}, Z. Zhendong^{2#}, S. Xiaoke^{3*}

¹Ningbo Yinzhou District Second Hospital, Ningbo, China
²Ningbo Second Hospital, Ningbo, China
³Cixi People's Hospital Medical and Health Group (Cixi People's Hospital), Cixi, China

Original article

*Corresponding author:

Zhou Xiaoshuai,

E-mail: sxk841201@163.com

Received: January 2024 Final revised: January 2024 Accepted: February 2024

Int. J. Radiat. Res., July 2024;

22(3): 719-725

DOI: 10.61186/ijrr.22.3.719

Keywords: Colorectal cancer, risk factors, postoperative pulmonary infection, meta-analysis, radiotherapy.

#Co-first authors, contributed equally to this work.

ABSTRACT

Background: Following surgery, lung infections are a frequent side effect that colorectal cancer patients experience and can be fatal. A meta-analysis was carried out to elucidate the risk variables for postoperative lung infection in patients with colorectal cancer. This information can help direct treatment and prevention strategies in clinical practice. Materials and Methods: Searches in PubMed, PMC, and other databases yielded clinical trials pertaining to aspects that increase the likelihood of postoperative lung infection in colorectal cancer patients. According to the abstract, key words, etc., literature screening. The Rev Man 5.4.1 was utilised to carry out a meta-analysis of the publications that fulfilled the grade requirements. Results: Finally, 10 studies were included, including 5165 patients with colorectal cancer, and the differences between infected and non-infected patients were analyzed. The results indicate that there were no risk factors for postoperative pulmonary infection in colorectal cancer patients based on age (95%CI (-23.16, 15.39), P = 0.69), TNM grade (95%CI (-0.06, 0.11), P = 0.56), operation time (95%CI (-0.02, 0.27), I2=89%, P=0.09), or COPD (95%CI (-0.01, 0.61), I2=98%, P=0.06). Factors that increase the likelihood of postoperative pulmonary infection in colorectal cancer patients include gender (95%CI [0.01,0.09]; P = 0.01), body mass index (95%CI [0.00,0.22]; P=0.04), surgical approach (95%CI [0.01,0.42]; P = 0.04), and a history of smoking (95%CI [0.06,0.34]; P=0.006). **Conclusion:** Clinical treatment and rehabilitation for colorectal cancer patients should take into account the multiple risk factors for lung infection following surgery, including gender, body mass index (BMI), surgical technique, and smoking history.

INTRODUCTION

The rectum or colon can become a tumorous growth, a condition known as colorectal cancer. Genetic mutations or abnormalities typically cause it by promoting the growth and spread of cells (1). This disease is a significant global health concern driven by genetic mutations and lifestyle factors (2). Amidst shifting dietary patterns and lifestyle colorectal cancer has risen to become the fifth leading cause of cancer death worldwide (3,4). This underscores the urgency of comprehensive research and intervention. Symptoms of colorectal cancer can include diarrhea, constipation, bloating, weight loss, nausea, vomiting, anal pain, and blood in the stool. These symptoms can also be a sign of other health problems (5). This emphasizes the complexity of colorectal cancer diagnosis.

When it comes to treating colorectal cancer, radiotherapy is crucial. Radiation therapy for colorectal cancer is a treatment that uses radiation to irradiate cancer cells to stop their growth and division by damaging their genetic material (DNA) ⁽⁶⁾. Radiotherapy acts directly or indirectly on the DNA of

tumor cells by producing ionizing radiation, such as X -rays or gamma rays. This action causes DNA strands to break, causing damage and eventually causing cancer cells to die or lose their ability to divide. The effects of radiotherapy on cancer cells mainly occur at specific stages of their life cycle, especially during the division phase ⁽⁷⁾. Because tumor cells divide at a relatively high rate, they are more sensitive to radiation. Although radiation therapy mainly affects cancer cells, it can also have a certain degree of impact on surrounding normal tissue. Treatment plans usually minimize damage to normal tissue ⁽⁸⁾.

Radiation can occasionally be administered prior to surgery in order to reduce the tumor's size, which in turn makes the surgery more manageable. This helps to reduce intraoperative or postoperative complications (9). For certain high-risk patients, postoperative radiotherapy can help reduce the risk of tumor recurrence after surgery. Radiotherapy can effectively reduce the local recurrence rate of colorectal cancer in the primary site and improve the therapeutic effect (10). Additionally, radiation therapy has the potential to aid in the prevention of cancer cell metastasis following surgery for some high-risk

individuals. Radiation therapy helps alleviate some of the tumor-related symptoms experienced by individuals with advanced colorectal cancer, including pain, bleeding, and nausea (11).

professionals can gain a better Medical understanding of colorectal cancer and its risks by studying the variables that increase the likelihood of postoperative lung infection in these individuals (12). It can help doctors better predict and control the occurrence and development of diseases, thus improving the survival rate and quality of life of patients (13). It also allows clinicians to tailor treatment strategies and implement targeted interventions. For patients with risk factors, doctors can take steps to reduce the risk of infection, such as enhanced care and better antibiotic treatment (14). For patients with no risk factors, doctors can predict their risk of infection, thereby preparing ahead of time to reduce the risk of infection (15). In order to better understand how to prevent postoperative lung infection in colorectal cancer patients, it is important to analyze the risk factors for this infection. Beyond its immediate clinical implications, this meta-analysis contributes substantively to broader public health awareness and scientific research development (16,17). The nature of lung infection can be better understood by examining its mechanism of action and the factors that influence risk factors. This will provide a stronger theoretical basis for the treatment and prevention of the disease (18).

In conclusion, the meta-analysis of postoperative pulmonary infection risk factors in colorectal cancer patients' post-radiotherapy serves as a nexus between clinical necessity and scientific advancement. This improves the level of disease cognition, guides clinical treatment, improves awareness of preventive measures, and promotes the development of scientific research. By integrating existing knowledge and introducing novel insights, this study endeavors to lay the foundation for improved treatment strategies, enhanced disease management, and a more profound understanding of the preventive measures required in this specific clinical context.

MATERIALS AND METHODS

Search strategy

(1) Colorectal cancer patient; (2) The infected group served as the experimental group, while the non-infected group served as the control group; (3) Age, TNM staging, operation time, chronic obstructive pulmonary disease (COPD), body mass index (BMI), surgical approach, and smoking history were all were tested.

Literature selection criteria

(1) Patients with colorectal cancer served as the

subjects; (2) the literature design type was a randomized controlled trial; (3) Random sequence generation; (4) Participants and personnel being blinded; (5) Incomplete outcome data; (6) No other bias.

Quality evaluation

Two research investigations independently screened and retrieved risk variables linked to postoperative pulmonary infection in colorectal cancer, and the results were qualitatively summarized. If the data extracted by two researchers is inconsistent, the third researcher will evaluate the solution.

Statistical analysis

Rev Man 5.41 was used to conduct the meta-analysis. A fixed effects model was used when there was no statistical heterogeneity among the studies, which occurred when P > 0.1 and I² < 50%. Studies were judged to have statistical heterogeneity when P < 0.1 and I² \geq 50%. Analyses using a random effects model, subgroup analysis was carried out concurrently with a test level of $\alpha=0.05$.

RESULTS

Systematic search results and study inclusion

In this study, 10 highly significant pieces of literature were obtained by searching for relevant literature and screening them, as shown in table 1. The table contains important indicators, the number of patients, the year of publication, and the initial author.

Table 1. Basic characteristics of the included literature involving experimental samples and indicators

Included literature	Number of Experimenta grou	al\Control	Indicators
ZHONG Jie 2022	97	590	Age, TNM staging, Operation time, Smoking history
Matteo Frasson 2016 (20)	148	954	TNM staging, BMI
YANG Yong 2017 (21)	41	352	Operation time, COPD, BMI, Smoking history
Chen Yicong 2019 (22)	23	134	Age, Operation time, BMI, Surgical method, Smoking history
Lu Xinquan 2018 ⁽²³⁾	85	739	Age, TNM staging, Opera- tion time, COPD, BMI, Surgical method, Smoking history
Yu Yue 2019 ⁽²⁴⁾	34	20	Age, TNM staging, COPD, BMI, Surgical method, Smoking history
ZHUANG Li- hong 2019 (25)	64	398	Operation time, BMI, Surgical method, Smoking history
Dai Yuan-qiang 2021 ⁽²⁶⁾	45	617	Age, Operation time, COPD, BMI, Smoking history
Wang Shixu 2019 ⁽²⁷⁾	60	512	Age, TNM staging, Operation time, COPD, Smoking history
Ding Ke 2018 (28)	34	218	Age, TNM staging, Operation time, Smoking history

Note: Tumour, node and metastasis (TNM), Body mass index (BMI), Chronic obstructive pulmonary disease (COPD).

The publication bias analysis

The findings of the evaluation of the aforementioned ten works of literature are displayed in figure 1. The findings demonstrated that the overall quality fulfilled the required standards, that a meta-analysis could be carried out, and that the analysis's conclusions were useful as a guide.

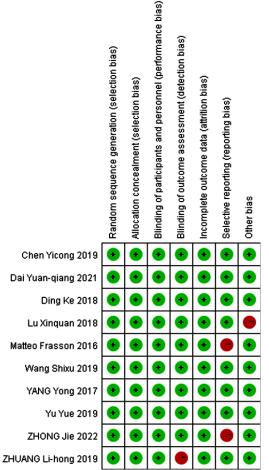


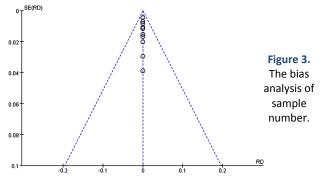
Figure 1. The publication bias analysis.

Meta-analysis results Patient characteristics

There were a total of 631 patients in the study's experimental group and 4534 patients in the control group, as shown in figure 2 of the meta-analysis. The study of heterogeneity in the number of patients between the two groups is presented in figure 3, and the findings indicate that there is no difference in the number of patients between the two groups (95% CI (-0.01, 0.01), P = 1.00).

	Experim	ental	Contr	ol		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Chen Yicong 2019	23	23	134	134	3.7%	0.00 [-0.06, 0.06]	
Dai Yuan-giang 2021	45	45	617	617	7.8%	0.00 [-0.03, 0.03]	
Ding Ke 2018	34	34	218	218	5.5%	0.00 [-0.04, 0.04]	
Lu Xinguan 2018	85	85	739	739	14.2%	0.00 f-0.02, 0.02l	
Matteo Frasson 2016	148	148	954	954	23.9%	0.00 (-0.01, 0.01)	+
Wang Shixu 2019	60	60	512	512	10.0%	0.00 (-0.02, 0.02)	
YANG Yong 2017	41	41	352	352	6.8%	0.00 (-0.03, 0.03)	
Yu Yue 2019	34	34	20	20	2.3%	0.00 (-0.08, 0.08)	
ZHONG Jie 2022	97	97	590	590	15.5%	0.00 [-0.01, 0.01]	
ZHUANG Li-hong 2019	64	64	398	398	10.3%	0.00 [-0.02, 0.02]	
Total (95% CI)		631		4534	100.0%	0.00 [-0.01, 0.01]	+
Total events	631		4534			,,	
Heterogeneity: Chi² = 0.0	0. df = 9 (P	= 1.00)	I2 = 0%				
Test for overall effect: Z =							-0.05 -0.025 0 0.025 0.05 Favours (experimental) Favours (control

Figure 2. The forest plot of sample number.



Determination of age and TNM grade as risk factors

Colorectal cancer patients were not more likely to develop a lung infection after surgery based on their age or TNM grade. As patients age, their immune system and lung structure and function change. Older people may have weakened immune systems, making them more susceptible to infections. In addition, older adults may also experience changes in lung structure and function, such as atrophy and a decrease in the number of alveoli, making the lungs less able to fight infection. The lower the overall staging value of TNM, the better the prognosis is generally expected. Therefore, the age and TNM of patients were analyzed, and the results are shown in figures 4 to 7. Neither the patients' ages nor their TNM grades were significantly different (95% CI (-0.06, 0.11), P = 0.56), ruling out these variables as potential risk factors.

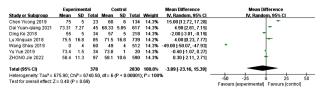


Figure 4. The forest plot of mean age.

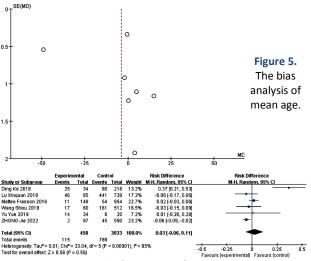
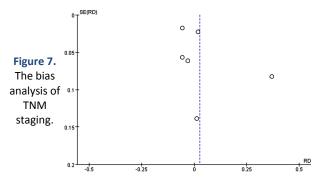


Figure 6. The forest map of TNM staging.

Determination of operative time and COPD as risk factors

In patients with colorectal cancer, postoperative

lung infection is not associated with either operating time or COPD. Extended surgical duration may result in excessive hemorrhage, and lung function is intimately linked to COPD. As a result, the two groups' variations in operation time and COPD were contrasted. The outcomes are displayed in figures 8 and 9. The groups did not differ statistically in terms of COPD (95% CI (-0.01, 0.61), I2=98%, P = 0.06) or operation time (95% CI (-0.02, 0.27), I2 = 89%, P = 0.09).



	Experim	ental	Cont	rol		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Chen Yicong 2019	8	23	31	134	11.0%	0.12 [-0.09, 0.32]	+
Dai Yuan-giang 2021	20	45	236	617	12.4%	0.06 [-0.09, 0.21]	
Ding Ke 2018	21	34	119	218	11.8%	0.07 (-0.10, 0.25)	
Lu Xinguan 2018	57	85	380	739	13.3%	0.16 [0.05, 0.26]	
Vang Shixu 2019	42	60	161	512	13.0%	0.39 [0.26, 0.51]	
ANG Yong 2017	27	41	131	352	12.3%	0.29 [0.13, 0.44]	_
ZHONG Jie 2022	43	97	386	590	13.3%	-0.21 (-0.32, -0.10)	
ZHUANG Li-hong 2019	34	64	161	398	12.8%	0.13 [-0.00, 0.26]	 •
Total (95% CI)		449		3560	100.0%	0.12 [-0.02, 0.27]	•
Total events	252		1605				
Heterogeneity: Tau2 = 0.0	4: Chi2 = 6	1.08. df	= 7 (P <	0.0000	1): P= 89	%	1 . J. J. J.
Test for overall effect: Z =					.,,		-1 -0.5 0 0.5 Favours (experimental) Favours (control)

Figure 8. The forest map of Operation time.

	Experim	ental	Contr	rol		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Dai Yuan-giang 2021	2	45	30	617	20.7%	-0.00 [-0.07, 0.06]	+
Lu Xinguan 2018	72	85	205	739	20.6%	0.57 [0.49, 0.65]	-
Wang Shixu 2019	40	60	112	512	20.2%	0.45 [0.32, 0.57]	
YANG Yong 2017	25	41	101	352	19.8%	0.32 [0.17, 0.48]	
Yu Yue 2019	12	34	4	20	18.6%	0.15 [-0.08, 0.39]	+-
Total (95% CI)		265		2240	100.0%	0.30 [-0.01, 0.61]	
Total events	151		452				
Heterogeneity: Tau ² = 0 Test for overall effect; 2			, df = 4 (F	° < 0.00	001); l²=	98%	-1 -0.5 0 0.5 Eavours (experimental) Favours (control)

Figure 9. The forest map of COPD.

Females with colorectal cancer

The risk of postoperative lung infection is reduced in females with colorectal cancer compared to males. Figures 10 and 11 show the results of a meta-analysis that demonstrated a much decreased risk of postoperative lung infection in female colorectal cancer patients compared to males. There was a statistically significant difference between the afflicted and unafflicted groups with respect to the percentage of male patients (95% CI (0.01, 0.09), P = 0.01). Colorectal cancer patients are more likely to get a lung infection after surgery if they are male.

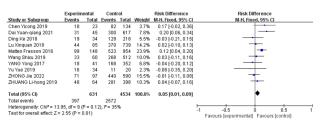
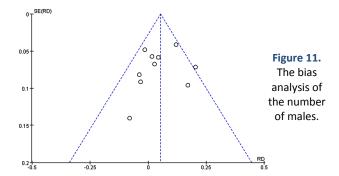


Figure 10. The forest plot of the number of males.



Other risk factors for postoperative lung infection

Other risk factors for postoperative lung infection in individuals with colorectal cancer include BMI, surgical technique, and smoking history. BMI values often reflect the degree of obesity in patients. Figure 12 demonstrates that there was a significant difference (95% CI (0.00,0.22), P = 0.04) between the experimental group and the control group with respect to the number of BMI > 24 patients. Generally, open surgery and laparoscopic surgery are included. As shown in figure 13, open surgery has a higher risk of infection (95% CI (0.01, 0.42), P = 0.04). Smoking lowers immunity and raises the possibility of illness. Figure 14 shows that colorectal cancer patients who smoke have a greater risk of postoperative lung infection than non-smoking patients (95% CI (0.06, 0.34), P = 0.006). Patients with colorectal cancer who smoke more heavily are also more likely to get a lung infection after surgery.

	Experim	ental	Contr	rol		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Chen Yicong 2019	16	23	114	134	11.6%	-0.16 (-0.35, 0.04)	
Lu Xinguan 2018	52	85	280	739	15.6%	0.23 [0.12, 0.34]	
Matteo Frasson 2016	11	148	31	954	17.9%	0.04 [-0.00, 0.09]	+
Wang Shixu 2019	45	60	284	512	15.2%	0.20 [0.08, 0.31]	-
YANG Yong 2017	28	41	166	352	13.7%	0.21 [0.06, 0.36]	_
Yu Yue 2019	20	34	4	20	9.8%	0.39 [0.15, 0.63]	
ZHUANG Li-hong 2019	9	64	80	398	16.3%	-0.06 [-0.15, 0.03]	
Total (95% CI)		455		3109	100.0%	0.11 [0.00, 0.22]	•
Total events	181		959				
Heterogeneity: Tau ² = 0.0	12; Chi* = 4	1.16, df	= 6 (P <	0.0000	1); [*= 85	%	-1 -05 0 05 1
Test for overall effect: Z=	2.01 (P = I	0.04)					-1 -0.5 0 0.5 1 Favours [experimental] Favours [control]

Figure 12. The forest map of BMI.

	Experim	ental	Cont	rol		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Chen Yicong 2019	18	23	88	134	24.1%	0.13 [-0.06, 0.31]	+
Lu Xinguan 2018	42	85	34	739	27.9%	0.45 (0.34, 0.56)	-
Yu Yue 2019	16	34	6	20	20.2%	0.17 [-0.09, 0.43]	+
ZHUANG Li-hong 2019	15	64	52	398	27.8%	0.10 [-0.01, 0.21]	-
Total (95% CI)		206		1291	100.0%	0.22 [0.01, 0.42]	-
Total events	91		180				
Heterogeneity: Tau2 = 0.0	34; Chi2 = 2	2.43, dt	= 3 (P <	0.0001); P = 879	6	1. de de de
Test for overall effect: 7 =	2.10 (P = 1	0.04)					-1 -0.5 0 0.5

Figure 13. The forest map of surgical method.

	Experime	ental	Cont	rol		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Chen Yicong 2019	9	23	38	134	9.8%	0.11 [-0.11, 0.32]	
Dai Yuan-giang 2021	8	45	133	617	11.7%	-0.04 [-0.15, 0.08]	-+
Ding Ke 2018	30	34	65	218	11.5%	0.58 [0.46, 0.71]	_
Lu Xinguan 2018	64	85	324	739	11.9%	0.31 [0.22, 0.41]	-
Wang Shixu 2019	42	60	137	512	11.6%	0.43 [0.31, 0.55]	_
YANG Yong 2017	27	41	155	352	11.0%	0.22 [0.06, 0.37]	
Yu Yue 2019	10	34	9	20	8.7%	-0.16 [-0.42, 0.11]	
ZHONG Jie 2022	53	97	292	590	11.8%	0.05 [-0.06, 0.16]	+-
ZHUANG Li-hong 2019	55	64	274	398	12.0%	0.17 [0.07, 0.27]	
Total (95% CI)		483		3580	100.0%	0.20 [0.06, 0.34]	•
Total events	298		1427				
Heterogeneity: Tau ² = 0.0	4; Chi2 = 8	6.75, dt	= 8 (P <	0.0000	1); I ² = 91	%	1 05
Test for overall effect Z=	2.75 (P = 0	(800.0					-1 -0.5 0 0.5

Figure 14. The forest map of smoking history.

DISCUSSION

One of the most prevalent malignant tumors of the digestive system, colorectal cancer has a devastating impact on human health. Surgery is the main method to treat colorectal cancer ⁽²⁹⁾. Pulmonary infection is a frequently occurring complication following surgery

in elderly patients diagnosed with colorectal cancer and it is a significant contributing cause to the deterioration and potential mortality of patients. Studies have suggested that postoperative pulmonary infection in elderly patients is influenced by multiple factors and caused by interaction, such as surgical trauma, long-term smoking history, previous chronic respiratory diseases, and old age and infirm (30). The result in figure 2 and 3 showed significant (P-value = 1.00) homogeneity of the number of patients used. The fatality rate of patients complicated with pulmonary infection after major abdominal surgery is relatively high, which can be as high as $10\% \sim$ 30%, which may be related to pulmonary infection significantly prolonging the hospital stay of patients, leading to the evolution of pathogenic bacteria, leading to multi-drug resistance and treatment difficulties, and multi-system co-infection and bacteremia (31). As patients age, their immune system and lung structure and function change. Older people may have weakened immune systems, making them more susceptible to infections. This could be deduced from figure 4 to 7, where age and TNM grade in patients were not considered as risk factors in older patients. In addition, older adults may also experience changes in lung structure and function, such as atrophy and a decrease in the number of alveoli, making the lungs less able to fight infection (32). When examining the senior group, a comparable report indicated a greater incidence of postoperative overall morbidity, but no disparities were seen in the risk of surgical complications (33). They also noted that elderly patients more frequently experience preoperative complications and emergency surgeries. Nevertheless, the rates of surgical morbidity following surgery are similar to those seen in younger patients.

Males with colorectal cancer are statistically more likely to experience a postoperative lung infection than females, as seen in figures 10 and 11, where the p-value is 0.01. Female with colorectal cancer have a lower risk of postoperative lung infection than men. This may be due to differences in immune systems and lung structure and function between men and female. Female's immune systems may be more sensitive, making them more susceptible to infection. However, female may have better lung structure and function than men, making it easier for them to fight off lung infections (34). The current research supports a data from the previous year that indicated women respond to immunological challenges with more antibody and cell-mediated immunity (35). Patients with colorectal cancer were not shown to be at increased risk for postoperative lung infection based on age, TNM grade, operation time, or COPD, according to our inferential results.

Smoking history is also a risk factor for postoperative lung infection in patients with colorectal cancer, as could be deduced from figure 14

with P-value of 0.006. Smoking damages a patient's immune system, making it more susceptible to infection (36). Our result is similar, where current or former smoker significantly increases the risk of major postoperative complications and mortality in veterans undergoing gastrointestinal cancer and thoracic surgeries (37). A recent report also concluded that individuals who smoke face a higher likelihood experiencing significant postoperative complications when compared to non-smokers (38). They therefore advise that it is crucial for clinicians and surgeons to communicate these surgical risks to smokers and emphasize the potential advantages of quitting smoking before undergoing major colonic resection. Furthermore, smoking can alter the way patients' lungs work and raise the likelihood of lung infections (39). Quitting smoking can reduce patients' risk of lung infections after surgery. Patients with colorectal cancer who drink alcohol are at a higher risk of developing a lung infection after surgery. Previous research has shown that CCL5-induced autophagy may be a mechanism by which prolonged alcohol use promotes colorectal cancer metastasis (40). Another study conducted by the Veterans Health Administration found that patients who drank more than two drinks daily in the days leading up to their lung resection procedure were more likely to experience difficulties after the procedure (41). Consuming alcoholic beverages lowers the body's natural defenses, making it more susceptible to diseases. In addition, alcohol consumption can increase the risk of lung infections by affecting the absorption and excretion functions gastrointestinal tract, leading to malnutrition and dehydration. Therefore, alcohol should be moderate, not excessive (42). In general, surgical technique, smoking history, and gender are risk factors for postoperative pulmonary infection in patients with colorectal cancer.

CONCLUSION

The study highlights that postoperative lung infection is a significant risk for elderly colorectal cancer patients. Factors such as gender, BMI, surgical method, and smoking history contribute to this risk. Notably, age and TNM grade are not considered risk factors in older patients. The findings emphasize the importance of addressing smoking and alcohol use to reduce complications in colorectal cancer surgeries.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are

available from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Authors' contributions: All authors contributed to the work equally.

REFERENCES

- Yoshimatsu K, Kono T, Ito Y, Satake M, Yamada Y, Okayama S, Yokomizo H, Shiozawa S. Laparoscopic Surgery Reduces Risk of Postoperative Complications and Non Cancer-related Survival in Patients Over 80 Years Old with Colorectal Cancer. Cancer Diagn Progn. 2021 Jul 3;1(4):297-301.
- Hossain MS, Karuniawati H, Jairoun AA, Urbi Z, Ooi DJ, John A & Hadi MA (2022). Colorectal cancer: a review of carcinogenesis, global epidemiology, current challenges, risk factors, preventive and treatment strategies. Cancers, 14(7), 1732.
- Lee KC, Chung KC, Chen HH, Cheng KC, Wu KL, Song LC. The impact of obesity on postoperative outcomes in colorectal cancer patients: a retrospective database study. Support Care Cancer. 2022;30(3):2151-2161.
- Kubi B, Nudotor R, Fackche N, Nizam W, Cloyd JM, Grotz TE, et al. Impact of Perioperative Blood Transfusions on Outcomes After Hyperthermic Intraperitoneal Chemotherapy: A Propensity-Matched Analysis. Ann Surg Oncol. 2021; 28(8):4499-4507.
- Abd El Aziz MA, Perry WR, Grass F, Mathis KL, Larson DW, Mandrekar J, Behm KT. Predicting primary postoperative pulmonary complications in patients undergoing minimally invasive surgery for colorectal cancer. *Updates Surg.* 2020;72(4):977-983.
- Carlos-Reyes A, Muñiz-Lino MA, Romero-Garcia S, López-Camarillo C & Hernández-de la Cruz ON (2021) Biological adaptations of tumor cells to radiation therapy. Frontiers in Oncology, 11, 718636.
- Abshire D and Lang MK (2018). The evolution of radiation therapy in treating cancer. In Seminars in oncology nursing, 34 (2): 151-157
- Wang K & Tepper JE (2021). Radiation therapy-associated toxicity: Etiology, management, and prevention. CA: a cancer journal for clinicians, 71(5): 437-454.
- Abraha I, Aristei C, Palumbo I, Lupattelli M, Trastulli S, Cirocchi R, et al. (2018). Preoperative radiotherapy and curative surgery for the management of localised rectal carcinoma. Cochrane Database of Systematic Reviews, 10: Cd002102.
- Osterman E, Hammarström K, Imam I, Osterlund E, Sjöblom T & Glimelius B (2020) Recurrence risk after radical colorectal cancer surgery—less than before, but how high is it? Cancers, 12(11), 3308.
- 11. Biller LH & Schrag D (2021). Diagnosis and treatment of metastatic colorectal cancer: a review. *Jama*, *325(7)*, *669-685*.
- 12. Aro R, Mäkäräinen-Uhlbäck E, Ämmälä N, Rautio T, Ohtonen P, Saarnio J, Meriläinen S. The impact of sarcopenia and myosteatosis on postoperative outcomes and 5-year survival in curatively operated colorectal cancer patients A retrospective register study. *Eur J Surg Oncol.* 2020;46(9):1656-1662.
- 13. Willadsen TG, Bebe A, Køster-Rasmussen R, Jarbøl DE, Guassora AD, Waldorff FB & Olivarius NDF (2016). The role of diseases, risk factors and symptoms in the definition of multimorbidity—a systematic review. Scandinavian Journal of Primary Health Care, 34 (2), 112-121.
- 14. Johnson KM, Newman KL, Green PK, Berry K, Cornia PB, Wu P, et al. Incidence and Risk Factors of Postoperative Mortality and Morbidity After Elective Versus Emergent Abdominal Surgery in a National Sample of 8193 Patients with Cirrhosis. Ann Surg. 2021;274 (4): e345-e354.
- Chao JS, Zhao SL, Ou-Yang SW, Qian YB, Liu AQ, Tang HM, et al. Post-transplant infection improves outcome of hepatocellular carcinoma patients after orthotopic liver transplantation. World J Gastroenterol. 2019; 25(37):5630-5640.
- Hu WH, Eisenstein S, Parry L, Ramamoorthy S. Preoperative malnutrition with mild hypoalbuminemia associated with postoperative mortality and morbidity of colorectal cancer: a propensity score matching study. *Nutr J.* 2019, 28;18(1):33.
- 17. Jin L, Zhang X, Deng L, Wu W, Shao W, Yin L, Lin R. Analysis of risk factors for concurrent pulmonary infection after operation for colon cancer. *J BUON.* 2019;**24**(2):436-441.

- Saadat LV, Fields AC, Lyu H, Urman RD, Whang EE, Goldberg J, Bleday R, Melnitchouk N. National Surgical Quality Improvement Program analysis of unplanned reoperation in patients undergoing low anterior resection or abdominoperineal resection for rectal cancer. Surgery. 2019;165(3):602-607.
- 19. ZHONG Jie, HE Yuhua, JIANG Lili, YANG Jie. Correlative factors analysis of pulmonary infection after laparoscopic colorectal resections for colorectal cancer. *Chinese Journal of Bases and Clinics in General Surgery, 2022, 22:218-24.*
- Frasson M, Granero-Castro P, Ramos Rodríguez JL, Flor-Lorente B, Braithwaite M, Martí Martínez E, et al. ANACO Study Group. Risk factors for anastomotic leak and postoperative morbidity and mortality after elective right colectomy for cancer: results from a prospective, multicentric study of 1102 patients. Int J Colorectal Dis. 2016;31(1):105-14.
- YANG Y, CHEN X, CHEN R, WANG X, FANG H, WANG H. Analysis of risk factors for postoperative pulmonary complications in colorectal cancer patients. *Journal of Practical Medicine*, 2017, 22:180.
- Chen Y, Liu Z, Liu D, Ji S, Xu J, You M (2019). Influencing factors and predictive value of pulmonary infection after colorectal cancer surgery. Chin J of Clinical Rational Drug Use, 55: 804-813.
- 23. Lu X, Xiaojiang YI, Dechang D, Wang W, Hongming LI, Zheng Y, et al. Risk factors for postoperative pulmonary infection in elderly patients with colorectal cancer after radical resection. J Dig On (colElectronic Version), September 2018, 15: 3375-3384.
- Yu Y. Analysis of risk factors of pulmonary infection after radical resection in elderly patients with colorectal cancer. World Latest Medical Information Abstracts 2019, 24: 436-441.
- Zuang L, Dong Y, Li X, Li M, Cai H. Prevalence and risk factors for postoperative pulmonary infection in 398 elderly patients with colorectal cancer from 2015 to 2019. Chin J Nosocomiol 2022; 8: e11664.
- Dai Yq, Xu Y, Wang C, et al. Risk Factors of Postoperative Pulmonary Complications after Radical Resection in Elderly Patients with Colorectal Cancer. J Med Res, 2021. 18:4.
- 27. Wang S and Xiang C. Characteristics and risk factors of pulmonary infection after laparoscopic radical resection of rectal cancer. Modern Digestion & Intervention 2019, Vol. Modern Digestion & Intervention 2019, vol. 24, No. 4.
- Numata T, Nakayama K, Fujii S, et al. Risk factors of postoperative pulmonary complications in patients with asthma and copd. BMC Pulmonary Medicine 2018; 18:4.
- Nobuhara H, Yanamoto S, Funahara M, Matsugu Y, Hayashida S, Soutome S, et al. Effect of perioperative oral management on the prevention of surgical site infection after colorectal cancer surgery: A multicenter retrospective analysis of 698 patients via analysis of covariance using propensity score. Medicine (Baltimore). 2018;97 (40): e12545.
- Lv C, Chen S, Shi T & Jia M (2022) Risk Factors Associated With Postoperative Pulmonary Infection in Elderly Patients With Hip Fracture: A Longitudinal Study. Clinical Nursing Research, 31(8), 1454-1461.
- 31. Jung J, Moon SM, Jang HC, Kang CI, Jun JB, Cho YK, Kang SJ, Seo BJ, Kim YJ, Park SB, Lee J, Yu CS, Kim SH. Incidence and risk factors of postoperative pneumonia following cancer surgery in adult patients with selected solid cancer: results of "Cancer POP" study. Cancer Med. 2018;7(1):261-269.
- 32. Sagawa M, Yoshimatsu K, Yokomizo H, Yano Y, Okayama S, Yamada Y, Usui T, Yamaguchi K, Shiozawa S, Shimakawa T, Katsube T, Kato H, Naritaka Y. Pulmonary Dysfunction Function and Poor Nutritional Status Are Risk Factors for Remote Infections Following Surgery for Colorectal Cancer. J Nippon Med Sch. 2018;85(4):208-214.
- Latkauskas T, Rudinskaitė G, Kurtinaitis J, Jančiauskienė R, Tamelis A, Saladžinskas Ž & Pavalkis D (2005) The impact of age on postoperative outcomes of colorectal cancer patients undergoing surgical treatment. BMC cancer, 5(1), 1-5.
- 34. Sims SM, Kao AM, Spaniolas K, Celio AC, Sippey M, Heniford BT, Kasten KR. Chronic immunosuppressant use in colorectal cancer patients worsens postoperative morbidity and mortality through septic complications in a propensity-matched analysis. *Colorectal Dis.* 2019;21(2):156-163.
- Reddy KD & Oliver BGG (2023). Sexual dimorphism in chronic respiratory diseases. Cell & Bioscience, 13(1), 1-16.
- Hu WH, Cajas-Monson LC, Eisenstein S, Parry L, Ramamoorthy S. Association of dialysis with adverse postoperative outcomes in colorectal cancer-an analysis of ACS-NSQIP. Int J Colorectal Dis. 2015;30(11):1557-62.
- 37. Gajdos C, Hawn MT, Campagna EJ, Henderson WG, Singh JA &

- Houston T (2012) Adverse effects of smoking on postoperative outcomes in cancer patients. *Annals of Surgical Oncology,* **19**, 1430 -1438
- 38. Badiani S, Diab J, Woodford E, Natarajan P & Berney CR (2022) Impact of preoperative smoking on patients undergoing right hemicolectomies for colon cancer. *Langenbeck's Archives of Surgery*, 407(5), 2001-2009.
- Kotlyarov S (2023). The Role of Smoking in the Mechanisms of Development of Chronic Obstructive Pulmonary Disease and Atherosclerosis. *International Journal of Molecular Sciences*, 24(10), 8725.
- Zhao H, Chen D, Cao R, Wang S, Yu D, Liu Y & Wang S (2018). Alcohol consumption promotes colorectal carcinoma metastasis via a CCL5-induced and AMPK-pathway-mediated activation of autophagy. Scientific reports, 8(1), 8640.
- Graf SA, Zeliadt SB, Rise PJ, Backhus LM, Zhou XH & Williams EC (2018) Unhealthy alcohol use is associated with postoperative complications in veterans undergoing lung resection. *Journal of Thoracic Disease*, 10(3), 1648.
- Ye C, Zhang G, Wang J, Chai Y. Histoplasmosis presenting with solitary pulmonary nodule: two cases mimicking pulmonary metastases. Niger J Clin Pract. 2015;18(2):304-6.