



E-ISSN: 2616-3470

P-ISSN: 2616-3462

© Surgery Science

www.surgeryscience.com

2025; 9(1): 05-09

Received: 10-10-2024

Accepted: 11-11-2024

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Correlation between smoking behaviour and surgical site infection on grade III colorectal cancer patients following elective colectomy

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DOI: <https://doi.org/10.33545/surgery.2025.v9.i1.A.1133>

Abstract

Introduction: Colorectal cancer is an accumulation of genetic mutation promoting excess proliferation of cells and inactivation of tumor suppressor genes causing neoplastic lesion and polyps to form on the colon and rectal epithelium. Smoking is one of the many risk factors which increases the risk of not only colorectal cancer formation but also post colectomy complications because of its carcinogenic components and wound healing disrupting properties. This study was done to determine the correlation between smoking behaviour and surgical site infection on grade III colorectal cancer patients following elective elective colectomy.

Method: This study is an analytic observational study with a retrospective cohort design. Data was collected by conducting an interview with patients undergoing treatment and from medical records in dr. Moewardi General Hospital with a total of 40 samples divided into 2 groups, 20 samples as the case group (smoker) and 20 samples as the control group (non-smoker). Data analysis was done using the fisher's exact test to evaluate correlation between age, gender, smoking status and smoking intensity with post-colectomy surgical site infection.

Result: The study did not find correlation between between age, gender, smoking status and smoking intensity with post-colectomy surgical site infection (p-value = 1.000; 0.677; 0.407; 0.219).

Conclusion: Smoking behavior did not influence the risk of post-colectomy surgical site infection.

Keywords: Colorectal cancer, smoking status, smoking intensity, surgical site

Introduction

Colorectal cancer is the accumulation of genetic mutation, causing uncontrolled cell proliferation and inactivation of tumor suppressor genes which may lead to lesions and polyps of the colon and rectum epithelial. In Indonesia, in the year 2021 alone, colorectal cancer is the fourth most common cancer, with 35.676 new cases and 19.2552. Risk factors for colorectal cancer can be divided into two groups, non-modifiable risk factors such as gender, age, genetics and family history and modifiable risk factors such as patient lifestyle, smoking, and alcohol consumption³. Smoking has been an ongoing health problem in Indonesia, with 36.3% of smokers in countries of ASEAN being Indonesian residents⁴. Not only has smoking been found to increase the risk of colorectal cancer incidence but also postoperative complications. Surgical site infections happen in 1.2 - 23.6 cases of 100 procedures. Smoking slow down wound healing process causing increased surgical site infection risk, longer hospitalization duration, increased need for blood transfusion and increased morbidity. Tissue hypoxia and vasoconstriction are the main mechanism of slowed wound closure and may cause complication and wound dehiscence⁵⁻⁷. This study is done to find correlation between smoking behavior and surgical site infection incidence after colectomy in stage III colorectal cancer patients in Dr. Moewardi General Hospital. The findings may hopefully be used as considerations in surgical preparations on patients with a history of smoking.

Materials and Methods

The study will be conducted as a retrospective cohort study with surgical site infection incidence as the outcome. There will be no medical intervention against patients. The subjects are patients undergoing treatment in Dr. Moewardi General Hospital, with a sample size of 40 patients.

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The samples will be divided into a case group of smokers (20 patients) and control group of non-smokers (20 patients). Consecutive sampling will be done with the inclusion criteria being Dr. Moewardi General Hospital stage III colorectal cancer patient, with a smoking history, and has done a colectomy surgery. Patients who did neoadjuvant therapy beforehand are excluded. The independent variable in this study is smoking status and smoking intensity and the dependent variable is surgical site infection cases. Data analysis will be done with SPSS program using the chi-square formula since both variables are nominal data. If not possible, Fisher's exact test will be used.

Results

Univariate analysis

Table 1: Sample Characteristics

Characteristic	Category	Frequency	Percentage (%)
Age	>65	13	32.5
	≤65	27	67.5
	Total	40	100.0
Gender	Female	17	42.5
	Male	23	57.5
	Total	40	100.0
Smoker	Yes	20	50.0
	Non-smoker	20	50.0
	Total	40	100.0
Smoking Intensity	Heavy	1	2.5
	Moderate	6	15.0
	Light	13	32.5
	Non-smoker	20	50.0
	Total	40	100.0
Surgical Site Infection	Yes	7	17.5
	No	33	82.5
	Total	40	100.0

Table 1 describes the characteristics of the samples included in this study. There was 13 patients over the age of 65 and 27 patients under the age of 65. The samples of smoking status included 20 smokers, all of which were male, and 20 non-smokers, all female. Regarding smoking intensity, 1 patient was classified as a heavy smoker, 6 moderate smokers, 13 light smokers and 20 non-smokers. Out of 40 samples, 7 surgical site infection cases were found.

Bivariate analysis

Table 2: Correlation between Age and Surgical Site Infection Post Colectomy

Age	Surgical Site Infection (Yes)	Surgical Site Infection (No)	Odds Ratio (95% CI)	p-value
>65	2	11		
≤65	5	22	0.800 (0.133 - 4.803)	1.000
Total	7	33		

This analysis was done using the Fisher's exact test. It shows 7 cases of post colectomy surgical site infection, 2 cases from >65 age group and 5 cases from ≤65 age group. Data analysis did not find significant correlation between the two variables (p-value = 1.000).

Table 3: Correlation between Gender and Surgical Site Infection Post Colectomy

Gender	Surgical Site Infection (Yes)	Surgical Site Infection (No)	Odds Ratio (95% CI)	p-value
Male	5	20	2.083 (0.352 - 12.320)	0.677
Female	2	15		
Total	7	33		

Table 3 shows post-colectomy surgical site infection occurred in 5 males and 2 females. Data analysis did not find significant correlation between the two variables (p-value = 0.677).

However, odds ratio score OF 2.083 determined males to be two times more likely to experience surgical site infection than females.

Table 4: Correlation between Smoking Status and Surgical Site Infection Post Colectomy

Smoking Status	Surgical Site Infection (Yes)	Surgical Site Infection (No)	Odds Ratio (95% CI)	p-value
Smoker	5	15	3.000 (0.507 - 17.740)	0.407
Non-smoker	2	18		
Total	7	33		

Table 4 shows post-colectomy surgical site infection occurred in 5 smokers and 2 non-smokers. Data analysis did not find significant correlation between the two variables (p-value = 0.407). An odds ratio of 3.000 can be interpreted as surgical site infections happening three times more likely in smokers.

Table 5: Correlation between Smoking Intensity and Surgical Site Infection Post Colectomy

Smoking Intensity	Surgical Site Infection (Yes)	Surgical Site Infection (No)	p-value
Light	3	10	0.219
Moderate	1	5	
Heavy	1	0	
Non-smoker	2	18	
Total	7	33	

Table 5 shows post-colectomy surgical site infection occurred in 3 light smokers, 1 moderate smoker, 1 heavy smoker, and 2 non-smokers. Data analysis did not find significant correlation between the two variables (p-value = 0.219).

Discussion

Sample Characteristics

This study included 40 samples, divided into 2 groups, case group consisting of 20 smokers and control group consisting of 20 non-smokers

Age

Data shows 13 patients were >65 years old and 27 patients were ≤65 years old. According to a study conducted by Sawicki *et al.* (2021), age has become a significant risk factor in colorectal cancer patients. Risk increases after the age of 50 years old and people become 3x more vulnerable at >65 years old [8]. Another study also supports this finding with 1.055.598 cases being patients >50 years old and 130.165 cases were patients <50 years old. However, it has become apparent that there is an increasing trend of colorectal cancer happening in patients <50 years old [9].

Gender

This study included 17 female samples and 23 male samples. Studies suggest that colorectal cancer is more common in males with 86.1 cases out of 100,000 people than females with 66.9 cases out of 100,000 people. Mortality seems to also be higher in male patients¹⁰. In male patients, colon cancer incidence is 36.7% and rectal cancer being 16.2% while in female patients, incidence rate of colon cancer is 29% and 10.1% for rectal cancer^[11].

Smoking Status

This study included 20 smokers and 20 non-smokers. Out of 20 smokers, all samples were recorded to be male. A survey of tobacco usage in Indonesia, Global Adult Tobacco Survey 2021, concluded the prevalence of male smokers to be 66.5 million people, 28 times that of female smokers, being 2.3 million people. A study also found smoking as a risk factor in colorectal cancer cases^[12].

Smoking Intensity

Smoking intensity was determined by score of brinkman index, 1-199 being light smoker, 200-599 as moderate smokers and a score of ≥ 600 as heavy smokers. Samples with a score of 0 is classified as non-smoker. Data shows 1 patient classified as heavy smoker, 6 patients as moderate smoker, and 13 patients as light smoker. Risk of colorectal cancer was found to increase along with intensity and duration of smoking^[12]. A study conducted in Japan found age >70 years old and brinkman index score >800 to be an independent risk factor of colorectal cancer in patients with underlying esophageal cancer^[13].

Correlation Analysis between Age and Incidence of Surgical Site Infection Post-Colectomy

Skin being the largest organ and main protection serving as a barrier from the outside world, its integrity must not be compromised. That is the reason for its great regenerative power. Skin healing is a series of events occurring on the wound site, including inflammation, proliferation and remodelling¹⁴. Physiology capacity is one of the major factors affecting wound healing which decreases with age, especially in geriatric patients (≥ 65 years old). Frailty syndrome and decreased skin regeneration cause delayed during wound healing and susceptibility to wound infections. Aging was also related to decreased immunity and increased risk of comorbidities¹⁵. Old skin produced less extracellular matrix and decreased blood circulation adds further to the already slow macrophage and T cell response in wound healing¹⁶. Hypoperfusion of wound tissue inhibit angiogenesis and epithel turn over. Older people also experience chronic inflammation causing constant high levels of cytokines such as interleukin-6 and TNF- α leading to fibrosis which inhibits re-epithalization^[17].

In this study, fisher's exact test was done to analyse the correlation between age and surgical site infection. The p-value of 1.000 show that there is no correlation between age and surgical site infection. A cohort study conducted by Agodi *et al.* (2015) did not find significance of age in the incidence of surgical site infection¹⁸. However, a larger study conducted on 650 patients undergoing knee arthroplasty found significant correlation between age and surgical site infection^[19].

Correlation Analysis between Gender and Incidence of Surgical Site Infection Post- Colectomy

Extracellular matrix consists of proteins forming cellular and tissue structure in the body.

Collagen as an extracellular matrix component has an important role in hemostasis, inflammation, and angiogenesis²⁰. Scarred skin showed increased production of collagen and elastin compared to normal skin. In men, collagen I, collagen VI and elastin production is higher than scarred skin of women. On the other hand, women have increased accumulation of collagen III²¹. Women also have increased immune response and antibody activity during mucosal healing which may be caused by difference in sexual hormones^[22]. Estrogen regulates activity of adenosine A2A receptor which modulate angiogenesis. An experiment on wild type female mice showed estrogen and adenosine A2A receptor to modulate VEGF expression and endothelial cell migration^[23]. Estrogen also reduced inflammation, increased extracellular matrix deposition and keratinocyte proliferation to promote wound closure^[24]. This study uses fisher's exact test to analyse correlation between gender and incidence of surgical site infection post-colectomy. The result did not find significance between the variables with p-value of 0.677. A study conducted by Langelotz *et al.* (2014) included 438,050 patients of which 8,639 were surgical site infection cases. Women were shown to have less risk of surgical site infection compared to men after an abdominal surgical procedure. The incidence rate of surgical site in women being 1.74/100 procedures and in men 2.26/100 procedures²⁵. Another study also found men to have higher risk of surgical site infection, especially after abdominal surgery^[26].

Correlation Analysis between Smoking Status and Incidence of Surgical Site Infection Post- Colectomy

Nicotine and carbon monoxide are the main component in cigarettes causing inhibition in wound healing. The main mechanism being tissue hypoxia and vasoconstriction leading to decreased tissue circulation. Carbon monoxide also has high affinity to hemoglobin and inhibit oxygen uptake. Hypoxia also happen due to decreased proliferation of red blood cell, white blood cell, and fibroblasts. Nicotine increase norepinephrine production and cause peripheral vasoconstriction. Platelet adhesion is also increased 100 fold increasing blood viscosity and form blood clots. Smoking inhibit cellular migration during inflammation and inhibit neutrophil and macrophage function in killing pathogen. Decreased pathogen detection and destruction may increase the risk of wound infection. Collagen synthesis in extracellular matrix is also decreased causing inhibition in re-epithalization^{6, 27, 28}. Hydrogen cyanide in cigarettes also inhibit enzymes responsible for oxygen transport and metabolism^[29].

Data was analyzed using fisher's exact test and the p-value was determined to be 0.407. This shows that the correlation between smoking status and surgical site infection is not significant. Another study showed significance between smoking and post-operative complication^[30].

Correlation Analysis between Smoking Intensity and Incidence of Surgical Site Infection Post-Colectomy

Long term smoking, 12-21 years was found to cause decreased bleeding time and faster whole blood clotting time²⁸. Problems in blood circulation and decreased inflammation response cause change in extracellular matrix metabolism. This increases the risk of necrosis, surgical site infection, hernia, delayed wound healing and wound dehiscence^[31]. Tar and nicotine also have immunosuppressive effects causing inhibition on phagocytosis and chemotaxis of immune cells^[32]. Smoking cessation as little as 4 weeks was found to decrease hospitalization duration and risk of wound healing problems³³. Smoking cessation also

caused recovery of tissue microenvironment and function of acute inflammation^[34].

Data analysis found no correlation between smoking intensity and surgical site infection with the p-value being 0.219. Even though studies found smoking to inhibit wound healing, this study cannot establish significant correlation between the variables.

Conclusion

This study did not find significant correlation between smoking status and post-colectomy surgical site infection in stage III colorectal cancer patients. Therefore, the initial hypothesis of the study cannot be accepted

Acknowledgments

I would like to express my deepest gratitude to faculty members and staff of Sebelas Maret University and Surgical Department of Dr. Moewardi General Hospital for facilitating and granting the permission to carry out this research.

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How to Cite This Article

Joe M, Budhi IBB, Nugroho AN, Suwardi. Correlation between smoking behaviour and surgical site infection on grade III colorectal cancer patients following elective colectomy. *International Journal of Surgery Science* 2025;9(1):05-09.

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