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*]

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

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***Corresponding author:**
Zhou Xiaoshuai,
***E-mail:** sxk841201@163.com*

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#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

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

Medical professionals can gain a better 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 $I^2 < 50\%$. Studies were judged to have statistical heterogeneity when $P < 0.1$ and $I^2 \geq 50\%$. 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 samples Experimental\Control group		Indicators
ZHONG Jie 2022 [19]	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, Operation 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).

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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.

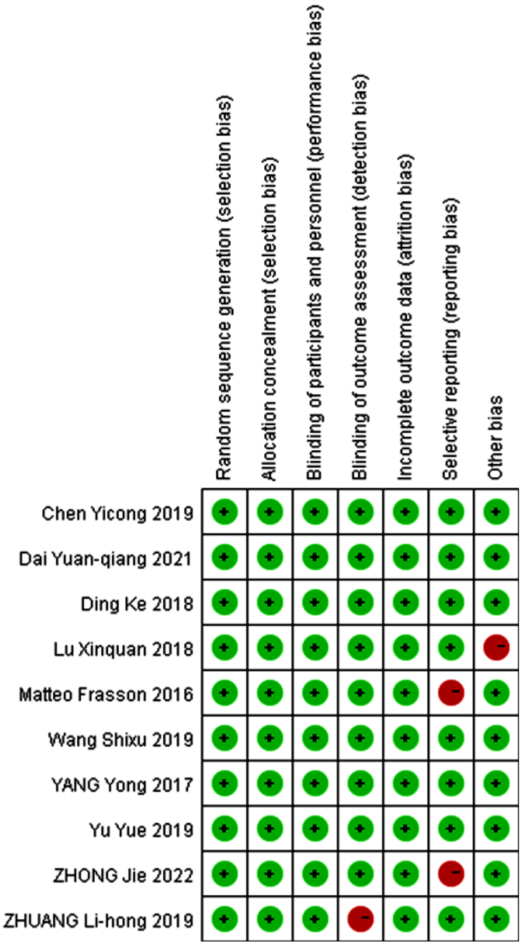

Figure 1. The publication bias analysis.

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).

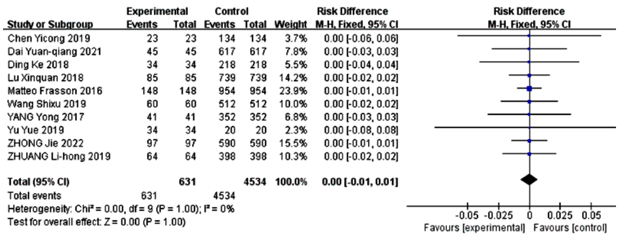

Figure 2. The forest plot of sample number.

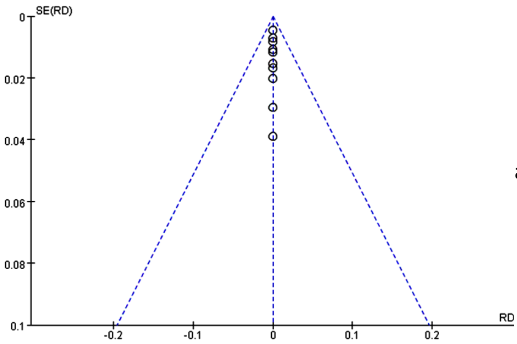

Figure 3. The bias analysis of sample number.

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.

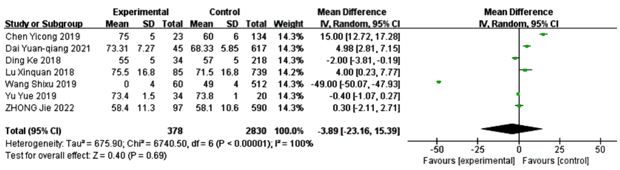

Figure 4. The forest plot of mean age.

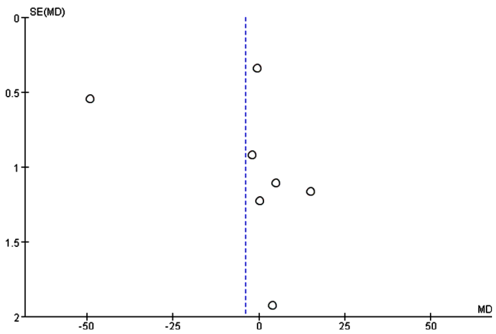

Figure 5. The bias analysis of mean age.

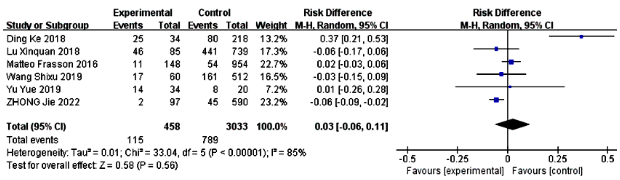

Figure 6. The forest map of TNM staging.

Determination of operative time and COPD as risk factors

In patients with colorectal cancer, postoperative

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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).

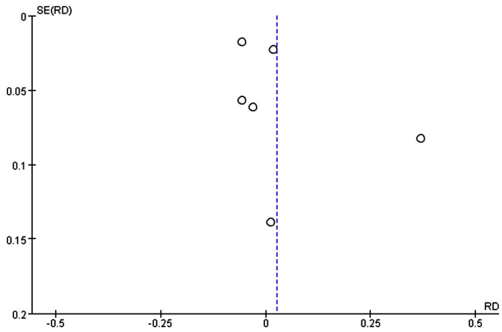

Figure 7. The bias analysis of TNM staging.

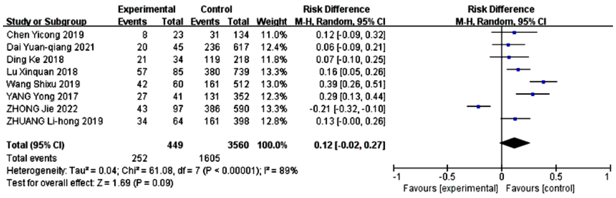

Figure 8. The forest map of Operation time.

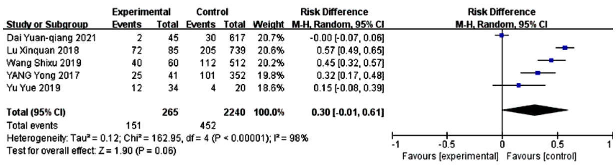

Figure 9. The forest map of COPD.

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.

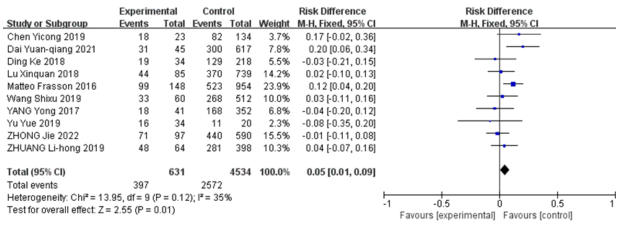

Figure 10. The forest plot of the number of males.

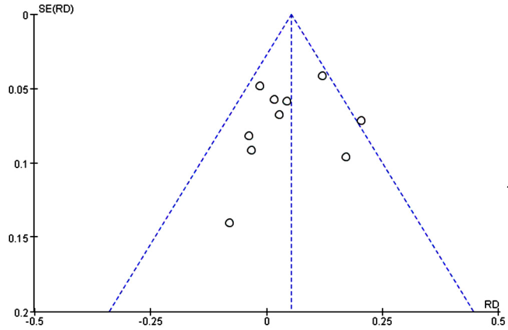

Figure 11. The bias analysis of the number of males.

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.

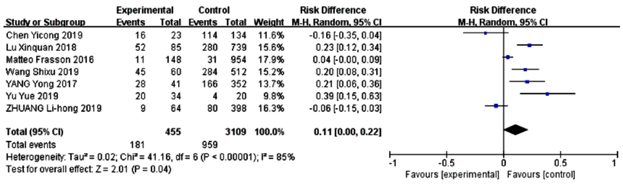

Figure 12. The forest map of BMI.

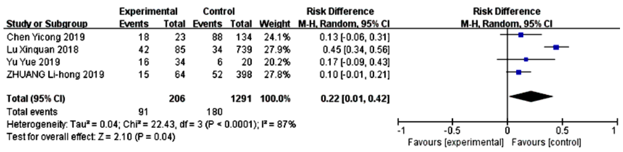

Figure 13. The forest map of surgical method.

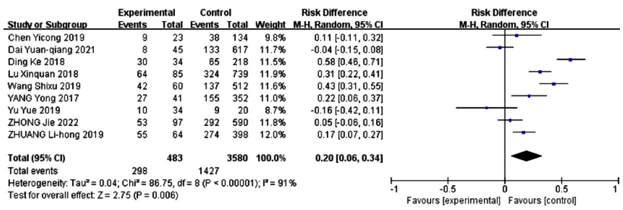

Figure 14. The forest map of smoking history.

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

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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% ~ 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 of 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 of the 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

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available from the corresponding author on reasonable request.

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

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