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Sevoflurane's inhibitory effect on postoperative colorectal cancer cell proliferation

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Abstract: **Background**: Surgical trauma and anesthesia may modulate the tumor microenvironment and influence postoperative recurrence in colorectal cancer (CRC). Volatile anesthetics such as sevoflurane have been reported to exert anti-tumor effects in vitro, yet their clinical impact on CRC cell proliferation and dissemination remains unclear. **Objectives**: To determine whether sevoflurane anesthesia attenuates early tumor cell activity compared with total intravenous anesthesia (TIVA) through assessment of circulating tumor cells (CTCs), systemic inflammation, and tissue biomarkers of proliferation and apoptosis. **Methods**: In this prospective, single-center, randomized controlled study, 80 CRC patients undergoing radical resection were allocated to sevoflurane (Group A, n = 40) or TIVA (Group B, n = 40). Peripheral blood was collected pre-operatively and on post-operative days (POD) 1, 3 and 7 for enumeration of CTCs (CellSearch®) and quantification of IL-6, TNF-α and C-reactive protein (CRP). Resected specimens were immunostained for Ki-67, PCNA, Bax, Bcl-2 and caspase-3. **Results**: Baseline characteristics were comparable. CTC counts rose after surgery in both groups but remained lower in Group A at every time-point (POD 3: 3.2±1.4 vs 4.5±1.7, P = 0.001). Inflammatory markers peaked on POD 3 but were significantly lower in Group A (IL-6: 40.1±9.5 vs 51.3±10.7 pg mL^{-1}, P < 0.001). Ki-67 and PCNA positive rates were reduced, whereas Bax/Bcl-2 ratio and caspase-3 expression were elevated in Group A (all P < 0.05). One-month CEA and CA19-9 levels did not increase in Group A, while they rose significantly in Group B (CEA: 4.9 ± 1.3 vs 6.1 ± 1.6 ng mL^{-1}, P = 0.007). **Conclusion**: These findings support the hypothesis that volatile anesthetics may reduce short-term recurrence risk and warrant larger, longer-term trials to validate oncological outcomes.

Keywords: Circulating tumor cells; Colorectal cancer; Inflammatory factors; Sevoflurane anesthesia; Tumor proliferation; Tumor markers

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INTRODUCTION

Colorectal cancer (CRC) is a globally prevalent malignancy, with its incidence increasing in both developed and developing countries (Xi *et al*., 2021; Zhou *et al*., 2021; Akimoto *et al*., 2021). CRC is characterized by significant morbidity and mortality rates. Despite advancements in surgical techniques and adjuvant therapies, the overall survival rate for CRC patients remains a significant public health concern (Hossain *et al*., 2022; Abedizadeh *et al*., 2024). Early detection and treatment are crucial for improving patient outcomes, with surgical resection continuing to be the primary treatment modality for CRC (Biller and Schrag, 2021). Surgical procedures necessitate the use of anesthetics and recent studies have highlighted potential concerns regarding the influence of anesthesia on cancer progression (Liu and Wang, 2022). Anesthetic agents, particularly those used during major surgeries like CRC resection, might affect tumor biology by influencing cell proliferation, migration and metastasis through complex mechanisms. Therefore, investigating the impact of different anesthetic agents on tumor biology, especially postoperatively, is now a critical area of research.

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Volatile anesthetics, including sevoflurane, are widely used in clinical practice due to their favorable pharmacokinetic and pharmacodynamic properties (Xie *et al*., 2022; Apai *et al*., 2021). These anesthetics generally demonstrate good tolerance, maintaining stable hemodynamic conditions and short recovery times, making them a favored choice for numerous surgical operations. However, accumulating evidence indicates that volatile anesthetics, particularly sevoflurane, may possess effects beyond simple anesthesia. Recent studies have uncovered potential antitumor properties of sevoflurane, suggesting it may inhibit the proliferation and metastasis of cancer cells. In vitro research has demonstrated that sevoflurane can influence the cell cycle and induce apoptosis in various cancer cell types, such as lung, breast and gastric cancer cells (Song and Tan, 2022; Fang *et al*., 2022). Additionally, sevoflurane has been shown to regulate immune response pathways within the tumor microenvironment, potentially enhancing its role as an adjunct in cancer therapy (Guo *et al*., 2024).

The effects of sevoflurane on colorectal cancer remain underexplored, with minimal research dedicated to its role in colorectal tumor biology. This anesthetic has been proposed to affect tumor-associated inflammation, immune cell function and protein expression linked to

tumor proliferation and apoptosis (Li *et al*., 2024). By modifying key signaling pathways like NF-κB, PI3K/Akt and MAPK/ERK, sevoflurane can potentially influence the tumor microenvironment, reducing postoperative recurrence and metastasis. Moreover, the impacts of sevoflurane on circulating tumor cells (CTCs) remain largely unexplored. CTCs, originating from primary tumors and entering the bloodstream, are crucial for cancer metastasis. Postoperative levels of CTCs are often used as biomarkers for cancer recurrence and metastasis. If sevoflurane can decrease CTC release, it may offer a new strategy to mitigate the risk of colorectal cancer recurrence post-surgery.

The postoperative period in CRC patients is crucial because this is when cancer recurrence is highly probable. Understanding how anesthesia impacts tumor cell behavior during this phase has significant clinical implications, especially concerning the prevention of recurrence and metastasis, which are major causes of death in CRC patients. This period is characterized by inflammatory responses, changes in immune function and alterations in the tumor microenvironment (Mishra *et al*., 2023). These factors may either promote or inhibit tumor growth and metastasis depending on their modulation. Consequently, the choice of anesthetic agent is a critical consideration in managing CRC patients undergoing surgery.

Given the potential impact of anesthetics on tumor biology, it is crucial to investigate whether certain anesthetic agents, such as sevoflurane, could potentially reduce postoperative cancer recurrence and metastasis (Liu and Wang, 2022). This study aims to explore the effects of sevoflurane on colorectal cancer surgery outcomes, focusing specifically on its ability to inhibit tumor cell proliferation, modulate inflammatory responses and regulate apoptosis. By analyzing these factors, we seek to gain a deeper understanding of the role of sevoflurane in influencing colorectal cancer recurrence. This research contributes to the existing knowledge on the role of anesthetics in cancer treatment and postoperative recovery and provides potential new strategies for optimizing anesthetic choices to improve the long-term outcomes for colorectal cancer patients. Sevoflurane, known for its anesthetic properties, also shows potential in modulating cancer progression. This study seeks to elucidate sevoflurane's impact on CRC biology. The research aims to provide new insights, potentially refining perioperative care strategies for cancer patients and improving their postoperative prognosis.

MATERIALS AND METHODS

Sample size calculation

This investigation employed a prospective and randomized design to evaluate the impact of various anesthetic agents on postoperative colorectal cancer (CRC) cell proliferation. The primary objective was to determine the inhibitory effects of sevoflurane on CRC cell proliferation following surgery. Sample size calculation was conducted using the G*Power software, based on previous research findings. Key assumptions included a significance level (α) of 0.05, a power (1-β) of 0.80 and a medium effect size (f = 0.25), which is commonly used in clinical studies involving biological interventions. Given these parameters, a minimum sample size of 36 patients per group was determined to ensure adequate statistical power.

To account for potential dropouts or incomplete data, an additional 10% was included, resulting in 40 patients per group. This approach ensured that the study had sufficient statistical power to detect significant differences between the two anesthesia methods. Consequently, a total of 80 patients were recruited, with 40 assigned to the sevoflurane anesthesia group (Group A) and 40 to the intravenous anesthesia group (Group B). These numbers were deemed appropriate for assessing the primary and secondary outcomes related to CRC recurrence, inflammatory markers and cell proliferation.

Grouping

Participants were randomly assigned to either the sevoflurane anesthesia group (Group A, n = 40) or the intravenous anesthesia group (Group B, n = 40). All participants underwent standard radical colorectal cancer surgery, which is a common treatment option for eligible CRC patients. Preoperative randomization was performed using a computer-generated random number table by an independent researcher to minimize selection bias. This process ensured comparability of baseline characteristics between the two groups and reduced the risk of confounding factors affecting the outcomes. Researchers conducting postoperative assessments were blinded to the anesthesia group assignments to prevent any bias in the evaluation of outcomes.

Inclusion and exclusion criteria

During the study, stringent criteria were established to ensure that only appropriate and representative patients were included. Specifically, the age range of participants was set from 18 to 75 years old, focusing on adult colorectal cancer patients undergoing surgery. Exclusion criteria targeted younger and elderly patients, as these groups may exhibit different responses to anesthesia and surgery. All participants were required to have primary colorectal cancer confirmed through histopathological evaluation and the tumor had to be resectable, excluding those in an advanced metastatic stage. Additionally, patients were classified according to the American Society of Anesthesiologists (ASA) grading system, with only those in ASA I to III being eligible due to their suitability for surgery with minimal systemic disease. Patients classified as ASA IV and V were excluded to avoid additional surgical and postoperative complications. Radical resection eligibility was another criterion, meaning that the surgical removal of the primary tumor and adjacent tissues to achieve clear margins was required. Preoperative

blood tests, including complete blood counts and liver and kidney function tests, had to be within normal or mildly abnormal limits. Severe preoperative abnormalities that could interfere with the study outcomes were grounds for exclusion. Informed consent was mandatory, ensuring all participants were fully aware of the nature of the study, potential risks and benefits.

The exclusion criteria also included patients with malignancies in organs other than the colon and rectum (CRC), as these could complicate the analysis of CRC outcomes. Participants who had previously received chemotherapy, radiotherapy, or targeted therapy were excluded to avoid the confounding effects of these treatments on tumor biology and immune function. Any history of allergy to anesthetic agents or contraindications to general anesthesia was grounds for exclusion to prevent adverse reactions. Patients with severe cardiopulmonary or central nervous system disorders were also excluded to reduce the risk of complications during surgery. Finally, individuals experiencing significant intraoperative complications or failing to undergo radical resection were not included in the study.

Outcome measures

The primary and secondary outcome measures were designed to assess the effects of anesthesia on CRC recurrence, tumor proliferation and inflammatory responses during the postoperative period.

Primary outcomes

Postoperative peripheral blood samples were collected on days 1, 3 and 7 to evaluate circulating tumor cell (CTC) counts. CTCs serve as a critical biomarker for predicting cancer recurrence and metastasis, as they can migrate from the primary tumor and establish metastases in other organs. Elevated CTC counts generally suggest a more adverse prognosis and a higher likelihood of recurrence. Serum levels of IL-6, TNF-α and CRP were assessed at specific postoperative time intervals. These inflammatory markers are frequently linked to inflammation and immune responses, which are crucial in the progression and recurrence of tumors. Higher levels of these markers are associated with worse postoperative outcomes, possibly indicating a tumor-promoting inflammatory environment. In tumor tissue samples collected during surgical procedures, the expression levels of Ki-67 and PCNA, indicators of cell proliferation, were evaluated. These proteins are extensively used to quantify the proliferative capacity of cancer cells and are strongly correlated with the aggressiveness and prognosis of tumors.

Secondary outcomes

Tumor recurrence biomarkers

One month after surgery, blood samples were collected to measure the serum levels of CEA and CA19-9. These biomarkers are commonly used in clinical practice to monitor CRC recurrence. Elevated levels of CEA and CA19-9 after surgery often signal tumor recurrence or metastasis.

Expression of apoptosis-related proteins in postoperative tumor tissue

The expression levels of Bcl-2, Bax and Caspase-3, which are involved in regulating apoptosis, were analyzed in postoperative tumor tissue. The balance between pro-apoptotic and anti-apoptotic proteins plays a crucial role in cancer cell survival and resistance to therapy.

Measurement methods

Postoperative peripheral blood samples of 5 mL were collected in EDTA tubes to inhibit clotting. CTCs were subsequently enriched and quantified using the CellSearch system, a widely used technique for tumor cell detection and analysis in blood samples. Processing was conducted according to the manufacturer's guidelines to ensure the accuracy and consistency of the results. Serum samples were isolated from whole blood via centrifugation and stored at -80°C until further analysis. Levels of IL-6, TNF-α and CRP were quantified using enzyme-linked immunosorbent assay (ELISA) kits. These kits were supplied by a certified provider and the tests were conducted according to the manufacturer's guidelines to ensure the reliability and reproducibility of the results.

- During surgery, tumor tissue samples were collected, fixed in 10% neutral-buffered formalin and embedded in paraffin. Sections were processed using immunohistochemistry (IHC) to evaluate the expression levels of Ki-67, PCNA, Bcl-2, Bax and Caspase-3. A pathologist assessed the intensity and extent of staining. Five high-power fields (400× magnification) per slide were randomly selected for evaluation. Protein expression quantification was conducted using Image-Pro Plus software.
- Tumor Biomarker Detection: One month after surgery, blood samples were collected for measurement of CEA and CA19-9 levels using chemiluminescent immunoassay analyzers. These assays are highly sensitive and provide accurate measurements of biomarker levels, which are critical for monitoring tumor recurrence.

Statistical analysis

Data analysis was conducted using SPSS version 26.0. Continuous variables were represented as means ± standard deviations ($\bar{x} \pm s$). Normality of data was evaluated using the Shapiro-Wilk test. Comparisons between groups for continuous variables were performed using independent sample t-tests. For repeated measures within groups, paired t-tests or repeated-measures analysis of variance (ANOVA) were applied, depending on the data structure. Categorical variables were expressed as frequencies and percentages and group differences were assessed using chi-square or Fisher's exact tests.

Correlations between continuous variables were analyzed using Pearson or Spearman rank correlation coefficients, depending on the data distribution. A P-value below 0.05 was considered statistically significant.

Ethical considerations

This study was approved by the institutional ethics committee and strictly followed the ethical principles stated in the Declaration of Helsinki. Before enrollment, all participants provided written informed consent, indicating their understanding of the study's objectives, procedures, risks and benefits. The research was conducted with the highest regard for patient safety, privacy and confidentiality. Additionally, all data were managed in accordance with relevant ethical and legal standards.

RESULTS

There were no statistically significant differences between the two groups in terms of gender, age, weight, ASA classification, tumor stage, or other baseline characteristics ($P > 0.05$), indicating that the two groups were well-balanced at baseline (table 1).

On the first, third and seventh postoperative days, the count of circulating tumor cells (CTCs) in both groups increased significantly compared to preoperative levels. However, the CTC count in Group A was significantly lower than in Group B ($P < 0.05$). Notably, on the third postoperative day, Group A exhibited a marked reduction in CTCs ($t = 3.671$, $P = 0.001$), indicating a potential inhibitory effect of sevoflurane on CTC release (table 2).

The serum levels of IL-6, TNF-α and CRP increased significantly postoperatively in both groups relative to preoperative levels. Notably, the levels of these inflammatory factors in Group A were significantly lower compared to those in Group B. On the third postoperative day, the inflammatory factor levels reached a peak, with Group A demonstrating a faster recovery rate than Group B (table 3).

In the postoperative tumor tissue, the expression rates of Ki-67 and PCNA in Group A were significantly lower compared to those in Group B (Ki-67: $t = 3.180$, $P = 0.003$; PCNA: $t = 3.029$, $P = 0.005$). Conversely, the ratios and levels of Bax/Bcl-2 and Caspase-3 were significantly higher in Group A (Bax/Bcl-2: $t = 3.518$, $P = 0.001$; Caspase-3: $t = 3.970$, $P = 0.001$) as detailed in table 4.

In the one-month follow-up, the levels of CEA and CA19-9 did not significantly increase in Group A, while they significantly increased in Group B (table 5).

DISCUSSION

This study investigates the influence of different anesthesia techniques on postoperative outcomes in colorectal cancer patients, with a focus on circulating tumor cell (CTC) counts, inflammatory cytokine levels and tumor tissue markers associated with proliferation and apoptosis. The findings suggest that sevoflurane anesthesia may reduce the risk of cancer recurrence by inhibiting postoperative cancer cell proliferation, decreasing CTC release, lowering inflammatory cytokine levels and modulating the expression of tumor tissue markers related to cell proliferation and apoptosis. These results highlight the potential of sevoflurane in mitigating tumor recurrence and metastasis following surgery.

Effects of sevoflurane on postoperative CTC release

The release of circulating tumor cells (CTCs) following surgery is a significant factor in cancer metastasis (Lin *et al*., 2021). CTCs originate from primary tumors and enter the bloodstream, potentially leading to the formation of secondary tumors at different sites (Gu *et al*., 2024). Therefore, CTCs are a key indicator for evaluating cancer recurrence. In our study, CTC counts were significantly higher on postoperative days 1, 3 and 7 compared to preoperative levels in both groups, which is consistent with the expected effects of surgery on tumor cell release. However, the sevoflurane group (Group A) exhibited significantly lower CTC levels at all time points compared to the intravenous anesthesia group (Group B). This suggests that sevoflurane may reduce the number of tumor cells released into the bloodstream postoperatively.

A potential explanation for this outcome involves sevoflurane's influence on the tumor microenvironment (Ishikawa *et al*., 2021). Volatile anesthetics like sevoflurane have been reported to inhibit angiogenesis, a critical process in tumor metastasis. By reducing the formation of new blood vessels, sevoflurane may limit the migration of tumor cells from the primary site into the bloodstream. Additionally, sevoflurane might suppress the degradation of the extracellular matrix, a necessary step for tumor cells to invade surrounding tissues and enter circulation. This effect may be enhanced by sevoflurane's impact on the immune system, particularly by increasing the activity of natural killer (NK) cells, which are crucial for recognizing and eliminating tumor cells (Konstantis *et al*., 2023). Our results align with previous research indicating that volatile anesthetics can decrease circulating tumor cells in the bloodstream, supporting the potential of sevoflurane in reducing the risk of postoperative metastasis and recurrence.

Sevoflurane's inhibitory effect on inflammatory cytokines

Surgical interventions, especially major operations like colorectal cancer surgery, trigger a substantial inflammatory response. This response can influence tumor progression and metastasis, as excessive inflammation can promote the survival and spread of cancer cells. In this study, we examined the levels of three key inflammatory markers-IL-6, TNF-α and CRP-on postoperative days 1

Table 1: Baseline characteristics of patients

Item	Sevoflurane anesthesia group (Group A, n=40)	Intravenous anesthesia group (Group B, n=40)	t/χ^2 value	P value
Gender (Male/Female)	22/18	20/20	0.181	0.671
Age (Years, $\bar{x} \pm s$)	61.5 ± 10.3	60.8 ± 9.7	0.237	0.813
Weight (kg, $\bar{x} \pm s$)	68.4 ± 8.2	67.9 ± 7.9	0.270	0.788
ASA Classification (I/II/III)	8/24/8	7/26/7	0.150	0.928
Tumor Stage (I/II/III)	10/20/10	9/22/9	0.158	0.924

Table 2: Peripheral blood ctcs count at different time points (per 5mL, $\bar{x} \pm s$)

Time point	Sevoflurane anesthesia group (Group A, n=40)	Intravenous anesthesia group (Group B, n=40)	*t* value	*P* value
Preoperative	2.5 ± 1.3	2.6 ± 1.2	0.313	0.755
Postoperative day 1	4.8 ± 1.5	5.6 ± 1.8	2.202	0.032
Postoperative day 3	3.2 ± 1.4	4.5 ± 1.7	3.671	0.001
Postoperative day 7	2.7 ± 1.2	3.6 ± 1.4	2.734	0.008

Table 3: Changes in inflammatory factor levels ($\bar{x} \pm s$)

Time point	Group	IL-6 (pg/mL)	TNF-α (pg/mL)	CRP (mg/L)	*t* value	*P* value
Preoperative	Group A	8.5 ± 2.4	15.3 ± 4.7	2.1 ± 0.8	0.391	0.696
	Group B	8.7 ± 2.5	15.8 ± 5.0	2.2 ± 0.9		
Postoperative day 1	Group A	35.2 ± 8.9	42.8 ± 10.5	14.7 ± 3.6	3.911	0.000
	Group B	42.5 ± 9.3	50.2 ± 12.1	18.3 ± 4.2		
Postoperative day 3	Group A	40.1 ± 9.5	48.7 ± 11.4	12.6 ± 3.2	4.275	0.000
	Group B	51.3 ± 10.7	60.4 ± 13.5	19.8 ± 4.7		
Postoperative day 7	Group A	20.5 ± 6.7	28.6 ± 7.8	6.3 ± 2.1	4.609	0.000
	Group B	29.7 ± 7.2	38.2 ± 9.3	9.8 ± 2.8		

Table 4: Expression of proliferation and apoptosis-related proteins in tumor tissue ($\bar{x} \pm s$)

Protein name	Sevoflurane anesthesia group (Group A, n=40)	Intravenous anesthesia group (Group B, n=40)	*t* value	*P* value
Ki-67 (Positive rate %)	35.2 ± 8.6	46.7 ± 10.3	3.180	0.003
PCNA (Positive rate %)	42.5 ± 9.1	53.4 ± 11.2	3.029	0.005
Bax/Bcl-2 ratio	1.92 ± 0.45	1.34 ± 0.37	3.518	0.001
Caspase-3 (OD value)	0.98 ± 0.21	0.71 ± 0.19	3.970	0.001

Table 5: Changes in tumor markers at one-month postoperative follow-up ($\bar{x} \pm s$)

Item	Sevoflurane anesthesia group (Group A, n=40)	Intravenous anesthesia group (Group B, n=40)	t value	P value
CEA (ng/mL)				
Preoperative	4.6 ± 1.2	4.8 ± 1.4	0.466	0.643
Postoperative 1 month	4.9 ± 1.3	6.1 ± 1.6	2.773	0.007*
CA19-9 (U/mL)				
Preoperative	18.7 ± 5.3	19.1 ± 5.7	0.370	0.712
Postoperative 1 month	19.8 ± 5.6	23.6 ± 6.4	3.249	0.002*

and 3. Both groups showed significantly higher levels of these cytokines compared to baseline, indicating an acute inflammatory response following surgery. The sevoflurane group exhibited significantly lower increases in inflammatory cytokines compared to the intravenous anesthesia group. Additionally, the sevoflurane group showed a faster recovery to baseline levels. These findings suggest that sevoflurane may possess anti-inflammatory properties that mitigate the inflammatory response related to surgery. Previous research indicates that sevoflurane can reduce the release of pro-inflammatory cytokines by inhibiting the NF-κB signaling pathway, a key regulator of immune responses and inflammation (Zhang *et al*., 2021). By suppressing the NF-κB pathway, sevoflurane decreases the activation of immune cells responsible for producing inflammatory cytokines, thereby alleviating postoperative inflammation. Sevoflurane also influences immune cell functions, potentially helping to maintain a balanced

immune response postoperatively. Volatile anesthetics, including sevoflurane, affect the activity of T lymphocytes, macrophages and dendritic cells. Controlling the inflammatory response and immune homeostasis is essential for reducing postoperative complications, including infections and tumor progression. These observations provide significant evidence of sevoflurane's anti-inflammatory benefits, contributing to improved recovery and long-term outcomes in colorectal cancer patients.

Sevoflurane's regulation of tumor tissue proliferation and apoptosis

Regulating tumor cell proliferation and apoptosis is essential for controlling cancer progression and metastasis. Tumor cells must avoid mechanisms of normal cell death, such as apoptosis, to continue growing and spreading. This study focused on the expression of proliferation markers, including Ki-67 and PCNA, as well as apoptosis markers, like Bax, Bcl-2 and Caspase-3, in tumor tissue collected postoperatively (Xu *et al*., 2022).

Our findings demonstrate that the sevoflurane group had significantly lower expressions of Ki-67 and PCNA compared to the intravenous anesthesia group. Ki-67 and PCNA are commonly used indicators of cell proliferation, typically linked to rapid tumor expansion and unfavorable prognosis. These results imply that sevoflurane could potentially suppress tumor cell proliferation by hindering cell cycle progression. Furthermore, the sevoflurane group displayed a significantly higher Bax/Bcl-2 ratio and Caspase-3 expression, indicative of enhanced tumor cell apoptosis.

The Bax/Bcl-2 ratio is a critical marker for apoptosis, with higher ratios generally facilitating apoptosis (Huwaimel *et al*., 2024). Caspase-3 serves as a key component in the apoptosis process and increased caspase-3 expression indicates the activation of cell death mechanisms (Eskandari and Eaves, 2022). Sevoflurane can induce apoptosis in tumor cells by modifying signaling pathways, such as the PI3K/Akt and ERK pathways, which play important roles in cell survival and proliferation. By inhibiting these pathways, sevoflurane may make tumor cells more susceptible to apoptosis, thereby limiting tumor growth and spread. These findings align with research suggesting that volatile anesthetics, including sevoflurane, may exhibit antitumor effects by reducing cell proliferation and enhancing cell death. This underscores the potential of sevoflurane as an additional therapy in cancer management, extending beyond its anesthetic benefits during surgical procedures.

Effects of sevoflurane on postoperative tumor marker levels

Tumor markers play a critical role in assessing the risk of cancer recurrence following surgical intervention. Specifically, carcinoembryonic antigens (CEA) and carbohydrate antigens 19-9 (CA19-9) levels are commonly used as indicators for colorectal cancer recurrence (Kamada *et al*., 2024; Alragig *et al*., 2024). In this study, one month post-surgery, the levels of CEA and CA19-9 were measured. The findings indicate that the sevoflurane group did not exhibit any significant increase in tumor marker levels compared to preoperative measurements. Conversely, the intravenous anesthesia group displayed a notable elevation in these markers. These results suggest that sevoflurane may contribute to the prevention of postoperative tumor recurrence through modulation of the tumor microenvironment, thereby restricting the release of tumor markers.

An increase in CEA and CA19-9 levels typically signifies heightened tumor cell activity. Studies indicate that sevoflurane can reduce the levels of these biomarkers, suggesting its potential to prevent cancer recurrence. The decrease in tumor marker levels implies a reduction in overall tumor burden among patients who have undergone sevoflurane anesthesia. These observations suggest that sevoflurane may offer additional benefits beyond its role as a general anesthetic, potentially improving long-term outcomes for patients undergoing colorectal cancer surgery.

Clinical significance of sevoflurane anesthesia

The research findings suggest that sevoflurane anesthesia demonstrates considerable potential in decreasing postoperative tumor recurrences and metastasis. Sevoflurane can reduce the release of circulating tumor cells, modulate levels of inflammatory cytokines, regulate tumor tissue proliferation and apoptosis and manage postoperative tumor marker levels. These attributes make sevoflurane a promising anesthetic choice for colorectal cancer patients. By influencing key mechanisms associated with cancer progression, sevoflurane may enhance postoperative survival rates and mitigate the risk of cancer recurrence.

The specific mechanisms underlying the antitumor effects of sevoflurane have not been fully deciphered. It is probable that a combination of factors, such as modulation of the tumor microenvironment, immune regulation and alterations in gene expression, contributes to its antitumor activity. Further investigation, including large-scale clinical trials and detailed molecular studies, is essential to clarify the precise mechanisms and clinical relevance of sevoflurane's role in cancer treatment.

Limitations and future outlook

Despite its promising findings, this study encounters several limitations. The sample size is relatively small, which may affect the generalizability of the results. Additionally, the follow-up period was restricted to one month, which is insufficient for assessing the long-term impact of sevoflurane on tumor recurrence and survival

rates. Furthermore, the influence of sevoflurane on different tumor stages and molecular subtypes of colorectal cancer remains unclear, necessitating further investigations to determine if sevoflurane's effects are consistent across various tumor types.

Future studies should address these limitations by designing multicenter trials with longer follow-up periods and larger sample sizes. Additionally, molecular biological approaches should be used to investigate the underlying mechanisms of sevoflurane's effects on cancer cells, including gene expression profiling, proteomics and epigenetic analysis. Such studies will help clarify whether sevoflurane can be utilized as a standard adjunctive treatment in cancer surgery to improve patient outcomes.

CONCLUSION

This study indicates that sevoflurane anesthesia may significantly alter postoperative outcomes in colorectal cancer patients by reducing the release of circulating tumor cells, modulating inflammatory cytokine levels and regulating tumor cell proliferation and apoptosis. These results imply that sevoflurane could potentially serve as a valuable tool for preventing postoperative cancer recurrence and enhancing patient survival. Further examination is required to validate these findings and to clarify the mechanisms through which sevoflurane exhibits its potential anticancer effects.

Informed consent statement

The data used in this study did not encompass any personal information about the participants. All data were utilized strictly for research purposes within this study and were handled with confidentiality to ensure no harm to the subjects. The Ethics Committee of Shanghai University of Traditional Chinese Medicine approved the study and exempted the need for informed consent due to the retrospective nature of the study and the absence of personal information in the data.

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Author's contributions

WU Qian designed the study, collected and analyzed the data, and drafted the manuscript. All authors read and approved the final manuscript.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval

This study was conducted in the Department of Anesthesiology, Hubei Cancer Hospital, Wuhan 430079, Hubei, China and was approved by the [Institutional Review Board Name] with Ethical Approval No. 202208121.

Conflict of interest

We declare that there is no conflict of interest regarding the publication of this document. We confirm that none of the authors have any financial or personal relationships that could inappropriately influence or bias the content of this work.

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