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**ABOUT COVER**

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The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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## Retrospective Study

## Effect of hyperthermia combined with opioids on cancer pain control and surgical stress in patients with gastrointestinal cancer

Jing Qian, Jing Wu, Jing Zhu, Jie Qiu, Chuan-Fu Wu, Cheng-Ru Hu

**Specialty type:** Gastroenterology and hepatology**Provenance and peer review:** Unsolicited article; Externally peer reviewed.**Peer-review model:** Single blind**Peer-review report's classification****Scientific Quality:** Grade B, Grade C**Novelty:** Grade B, Grade B**Creativity or Innovation:** Grade B, Grade C**Scientific Significance:** Grade B, Grade C**P-Reviewer:** Altuna SC; Lengyel CG**Received:** August 6, 2024**Revised:** August 27, 2024**Accepted:** August 28, 2024**Published online:** December 27, 2024**Processing time:** 113 Days and 1.2 Hours**Jing Qian, Jing Wu, Jing Zhu, Cheng-Ru Hu**, Department of Oncology, Suzhou Ninth People's Hospital, Suzhou 215200, Jiangsu Province, China**Jie Qiu, Chuan-Fu Wu**, Department of Gastrointestinal Surgery, Suzhou Ninth People's Hospital, Suzhou 215200, Jiangsu Province, China**Corresponding author:** Cheng-Ru Hu, MM, Associate Chief Physician, Department of Oncology, Suzhou Ninth People's Hospital, No. 2666 Ludang Road, Taihu New Town, Wujiang District, Suzhou 215200, Jiangsu Province, China. [huchengru1218@163.com](mailto:huchengru1218@163.com)**Abstract****BACKGROUND**

Surgical palliative surgery is a common method for treating patients with middle and late stage gastrointestinal tumors. However, these patients generally experience high levels of cancer pain, which can in turn stimulate the body's stress and undermine the effect of external surgery. Although opioid drugs have a significantly positive effect on controlling cancer pain, they can induce adverse drug reactions and potential damage to the body's immune function. Hyperthermia therapy produces a thermal effect that shrinks tumor tissues. However, its effect on relieving the pain of middle and late stage gastrointestinal tumors but also the stress of surgical palliative surgery remains unclear.

**AIM**

To investigate the effect of hyperthermia combined with opioids on controlling cancer pain in patients with middle and late stage gastrointestinal cancer and evaluate its impact on surgical palliative surgical stress.

**METHODS**

This was a retrospective study using the data of 70 patients with middle and late stage gastrointestinal tumors who underwent cancer pain treatment and surgical palliative surgery in the Ninth People's Hospital of Suzhou, China from January 2021 to June 2024. Patients were grouped according to different cancer pain control regimens before surgical palliative surgery, with  $n = 35$  cases in each group, as follows: Patients who solely used opioid drugs to control cancer pain were included in Group S, while patients who received hyperthermia treatment combined with opioid drugs were included in Group L. In both groups, we compared the effectiveness of cancer pain control (pain score, burst pain score, 24-hour burst pain frequency, immune function, daily dosage of opioid drugs, and

adverse reactions), surgical palliative indicators (surgery time, intraoperative bleeding, stress response), and postoperative recovery time, including first oral feeding time, postoperative hospital stay).

## RESULTS

Analgesic treatment resulted in a significant decrease in the average pain score, burst pain score, and 24-hour burst pain frequency in both Groups L and S; however, these scores were statistically significantly lower in Group L than in Group S group ( $P < 0.001$ ). Analgesic treatment also resulted in significant differences, namely serum CD4<sup>+</sup> ( $29.18 \pm 5.64$  vs  $26.05 \pm 4.76$ ,  $P = 0.014$ ), CD8<sup>+</sup> ( $26.28 \pm 3.75$  vs  $29.23 \pm 3.89$ ,  $P = 0.002$ ), CD4<sup>+</sup>/CD8<sup>+</sup> ( $0.97 \pm 0.12$  vs  $0.83 \pm 0.17$ ,  $P < 0.001$ ), between Group L and Group S, respectively. The daily dosage of opioid drugs incidence of adverse reactions such as nausea, vomiting, constipation, and difficulty urinating were statistically significantly lower in Group L than those in group S ( $P < 0.05$ ). Furthermore, palliative surgery time and intraoperative blood loss in Group L were slightly lower than those in Group S; however, the difference was not statistically significant ( $P > 0.05$ ). On the first day after surgery, serum cortisol and C-reactive protein levels of patients in group L and group S were  $161.43 \pm 21.07$  vs  $179.35 \pm 27.86$   $\mu\text{g/L}$  ( $P = 0.003$ ) and  $10.51 \pm 2.05$  vs  $13.49 \pm 2.17$   $\text{mg/L}$  ( $P < 0.001$ ), respectively. Finally, the first oral feeding time and hospitalization time after surgery in group L were statistically significantly shorter than those in group S ( $P < 0.05$ ).

## CONCLUSION

Our findings showed that hyperthermia combined with opioids is effective in controlling cancer pain in patients with middle and late stage gastrointestinal tumors. Furthermore, this method can reduce the dosage of opioids used and minimize potential adverse drug reactions, reduce the patient's surgical palliative surgical stress response, and shorten the overall postoperative recovery time required.

**Key Words:** Thermal therapy; Opioid drugs; Gastrointestinal tumors; Cancer pain; Surgical operation

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**Core Tip:** Cancer pain can stimulate the body stress of cancer patients, thereby prolonging recovery time after surgery. The present study found that hyperthermia combined with opioids had a significant effect on cancer pain control in patients with middle and late stage gastrointestinal tumors, reducing the surgical palliative surgical stress response and shorten the postoperative recovery time. This not only provides a novel direction for analgesia in patients with middle and late stage gastrointestinal tumors, but also has important guiding significance for the study of perioperative plans in these patients.

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## INTRODUCTION

All gastrointestinal tumors, including gastric cancer, rectal cancer, and colon cancer, are malignant tumors of the digestive system. In recent years, the incidence rate of gastrointestinal tumors has gradually increased, rendering them an important public health issue that seriously affects people's lives and health[1]. For middle and late stage gastrointestinal tumors, surgical palliative resection can be adopted, thereby improving the quality of life for cancer patients and extending their survival period. Previous research showed that the incidence of cancer-related pain in patients with middle and late stage tumors can reach 38%-66.4%[2], and there is a potential for sudden and severe pain outbreaks at any time[3]. Cancer pain, as an intolerable symptom of poor control, not only does it affect the comfort of patients, but it can also induce a series of side effects such as elevated blood pressure, increased heart rate, and weakened immune system, thereby stimulating the body's stress and affecting the patient's surgical palliative surgery. Currently, oral opioids are the most commonly used treatment for cancer pain[4]. Opioid analgesia reduces pain responses by activating different neurotransmitter systems, such as norepinephrine and serotonin, during the treatment, the drug dose was increased according to the severity of the patient's cancer pain, most patients' cancer pain can be temporarily relieved. However, when gastrointestinal tumors develop to middle and late stages of tumor cachexia, they cause gastrointestinal discomfort and decreased digestive ability, leading to poor digestion and absorption. Moreover, an increase in the dose of opioid drugs can easily induce adverse drug reactions, resulting in poor analgesic effects. Therefore, on the basis of maintaining moderate doses of opioid drugs, alternative analgesic methods should be considered to enhance analgesic efficacy and reduce the incidence of adverse reactions[5].

Hyperthermia therapy is a purely physical medical treatment that produces thermal effects in human tissues using artificial means. This method exposes the tumor lesion to high temperatures and longer heat storage time, thereby

inducing cytotoxic and biological effects[6], killing tumor cells, and relieving the pain reaction caused by tumor compression[7]. The aim of the present study was to investigate the effect of a combination therapy consisting of hyperthermia and opioids on cancer pain in patients with middle and late stages of gastrointestinal tumor development. Furthermore, this study intended to assess the impact of this approach on patients undergoing palliative surgical stress, thereby providing reference for the clinical treatment of patients with middle and late stages gastrointestinal tumors.

## MATERIALS AND METHODS

### Research subjects

In this retrospective study, we collected data from 70 patients with gastrointestinal tumors who underwent cancer pain treatment and palliative surgery at Suzhou Ninth People's Hospital, China from January 2021 to June 2024. Patients were included if they (1) Were diagnosed with middle and late stages of gastrointestinal tumors through pathological examinations, and presented with moderate to severe cancer pain, with a pain number rating (NRS) of  $\geq 4$  points; (2) Received palliative surgical treatment; and (3) Their expected survival time before surgery was  $\geq 1$  month. Exclusion criteria were as follows: (1) Serious adverse reactions to opioid drugs; (2) Contraindications to hyperthermia; (3) Presence of other primary malignant tumors, in addition to gastrointestinal malignant tumors; (4) Speech communication disorders or/and abnormal consciousness; (5) Associated with other causes of body pain; and (6) Other anti-tumor treatments, such as chemotherapy or targeted therapy, have been received before surgery.

### Analgesic method

Patients were divided into two groups according to different cancer pain control regimens before surgical palliative surgery, with  $n = 35$  cases in each group.

Group S: Only opioid drugs were administered to treat cancer pain. According to the three-step drug analgesic treatment guidelines for cancer pain issued by the World Health Organization, step by step medication was administered according to the degree of pain[8]. Patients with moderate pain (NRS scores 4-6) were given tramadol sustained-release tablets (manufacturer: China Granday Pharmaceutical Co., Ltd., specification: 100 mg/tablet, 10 tablets per box) orally every 12 hours. Patients with severe pain (NRS score 7-10) were given oral hydrocodone hydrochloride sustained-release tablets (manufacturer: China Mengdi Pharmaceutical Co., Ltd., specification: 10 mg/tablet, 10 tablets per box) every 12 hours. All patients were treated for seven days and completed one course of analgesic treatment.

Group L: Patients in this group were treated with a combination therapy of oral opioids and intraperitoneal endogenous field hyperthermia (Jilin Changchun Mida, model NRL-III). The specific operation method was as follows: A total of six temperature measuring electrodes were placed on the skin and rectum of the patient, in accordance with the tumor location. Body temperature was controlled in the range of 41.0 °C-43.0 °C by the computer system of the hyperthermia machine, and each operation lasted for 45 minutes. Hyperthermia treatment was performed once every day. All patients received a 7-day course of pain relief treatment, and all patients completed one course of pain relief treatment.

### Surgical methods

Patients with gastrointestinal cancer completed a course of cancer pain relief after treatment. According to the tumor's condition, palliative surgery was performed under laparoscopy. Palliative surgery for middle and late stages gastric cancer mainly involves the removal of the primary lesion, including distal gastrectomy, proximal gastrectomy, total gastrectomy, and combined organ resection. Furthermore, palliative surgery for middle and late stages rectal and colon cancer aims to remove the primary lesion as completely as possible. However, if surgery cannot completely remove the primary lesion, intestinal ostomy, intestinal side-to-side anastomosis, partial intestinal resection, and prophylactic intestinal ostomy should be performed according to the actual situation of the patient. Examples include simple small intestine stoma, simple colon stoma, ileocolonic anastomosis, ileocolonic anastomosis, partial small intestine or colon resection anastomosis, and even simple and practical small intestine or colon ostomy tube.

### Observation indicators

(1) Baseline data characteristics: Patients' characteristics between the two groups, such as age, body mass index, gender, type of gastrointestinal tumor, pathological grading of primary tumor, maximum diameter of primary tumor, major distant metastatic organs, and degree of cancer pain, were evaluated; (2) Cancer pain control effect: The patients' cancer pain was evaluated using NRS, with 0 indicating no pain, 1-3 indicating mild pain, 4-6 indicating moderate pain, and 7-10 indicating severe pain. The average pain score, burst pain score, and 24-hour burst pain frequency of the two groups of patients were noted before and after one course of pain relief treatment; five mL of venous blood were collected from both groups before and after one course of pain relief treatment. After high-speed centrifugation, the upper serum was separated and obtained. Furthermore, flow cytometry (Beckman Coulter, model: CytoFLEX) was used to detect T lymphocyte subsets ( $CD4^+ CD8^+$ ,  $CD4^+/CD8^+$ ); the daily dosage of opioids and the incidence of adverse reactions in both groups were observed, including nausea and vomiting, constipation, dizziness and drowsiness, delirium and hallucinations, dysuria, respiratory depression, and other adverse reactions; (3) Surgical indicators: Surgical palliative operation indexes of gastrointestinal tumor, including operation time, intraoperative blood loss, and surgical stress response, were registered in both groups, Among them, the detection of surgical stress response indicators was carried out by collecting 5 mL of venous blood from patients on the first day after surgery. In addition, enzyme linked immunosorbent assay was used to detect the expression levels of cortisol (COR) and C-reactive protein (CRP) in serum; and (4) Postoperative

recovery time: In both groups, we noted the first oral feeding time and postoperative hospitalization time after surgery.

### Statistical analysis

SPSS 26.0 software was used for statistical analysis. All measurement data were expressed as mean  $\pm$  SD, and *t*-test was performed to compare the two groups. Count data were expressed as a percentage (%), and the two groups were compared using the  $\chi^2$  test. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

### Comparison of baseline data between the two groups

As shown in [Table 1](#), the comparison between the two groups revealed no statistical significant differences in age, body mass index, sex, type of gastrointestinal tumor, pathological grading of primary tumor, maximum diameter of primary tumor, major distant metastatic organs, and degree of cancer pain ( $P > 0.05$ ) ([Table 1](#)).

### Comparison of cancer pain between the two groups before and after analgesic treatment

Comparisons of the average pain score, burst pain score, and 24-hour burst pain frequency between the two groups before pain relief treatment, differences did not reveal any statistically significant differences ( $P > 0.05$ ). After analgesic treatment, all indices were significantly reduced, and the Group L was lower than the Group S. All differences were statistically significant ( $P < 0.001$ ) ([Table 2](#)).

### Comparison of immune function indicators between the two groups before and after pain relief treatment

Comparison of CD4<sup>+</sup>, CD8<sup>+</sup>, and CD4<sup>+</sup>/CD8<sup>+</sup> indicators before analgesic treatment, showed no statistically significant differences between two groups of gastrointestinal tumor patients ( $P > 0.05$ ). Analgesic treatment also resulted in significant differences, namely serum CD4<sup>+</sup> ( $29.18 \pm 5.64$  vs  $26.05 \pm 4.76$ ,  $P = 0.014$ ), CD8<sup>+</sup> ( $26.28 \pm 3.75$  vs  $29.23 \pm 3.89$ ,  $P = 0.002$ ), CD4<sup>+</sup>/CD8<sup>+</sup> ( $0.97 \pm 0.12$  vs  $0.83 \pm 0.17$ ,  $P < 0.001$ ), between Group L and Group S, respectively ([Table 3](#)).

### Comparison of daily dosage and incidence of adverse reactions of opioid drugs between the two groups

The daily dosage of opioid drugs in Group L was significantly lower than that in Group S, and the incidence of adverse reactions, such as nausea, vomiting, constipation, and difficulty in urinating, was lower than that in Group S. All differences were statistically significant ( $P < 0.05$ ) ([Table 4](#)).

### Comparison of surgical palliative surgical indicators between the two groups

The surgical time and intraoperative bleeding in Group L were slightly lower than those in Group S; however, the difference was not statistically significant ( $P > 0.05$ ). On the first day after surgery, serum COR and CRP levels of patients in group L and group S were  $161.43 \pm 21.07$  vs  $179.35 \pm 27.86$  ug/L ( $P = 0.003$ ) and  $10.51 \pm 2.05$  vs  $13.49 \pm 2.17$  mg/L, ( $P < 0.001$ ), respectively ([Table 5](#)).

### Comparison of postoperative recovery time between the two groups

The first oral feeding time and hospitalization time after surgery in group L were significantly shorter than those in group S, and the difference was statistically significant ( $P < 0.05$ ) ([Table 6](#)).

## DISCUSSION

Cancer pain often occurs during the middle and late stages of malignant tumors[9]. Opioids are the preferred drugs for alleviating moderate to severe cancer pain[10]. In this study, we used tramadol and oxycodone hydrochloride sustained-release tablets, which are opioid receptor agonists, with pharmacological characteristics of two-phase absorption and controlled release function. Their analgesic effect lasts for a significant time, can maintain a stable blood drug concentration, and can quickly and efficiently relieve moderate to severe cancer pain[11]. However, there is a potential sudden increase in cancer pain due to the growing condition of patients with gastrointestinal tumors, rendering an increase in the administered dose often necessary to achieve the desired analgesic effect. Previous studies found that the adverse reactions and addictive nature of opioid drugs increase with drug escalation and dosage increase[12]. Consequently, a simple increase in the dosage of opioid drugs might not be the optimal solution.

Hyperthermia is a novel method that refers to the use of local heating to treat tumors[13]. As a new generation of hyperthermia system, endogenous field hyperthermia can not only directly kill tumor cells, but also reduce the excitability of sensory nerves with concurrent analgesic effects. For instance, Yue *et al*[14] found that abdominal thermotherapy could effectively relieve pain. However, the specific mechanism by which thermal therapy alleviates pain is currently unclear.

Nonetheless, the results of the present study showed that the average pain score, burst pain score, and 24-hour burst pain frequency after pain relief treatment in patients receiving a combination of thermal therapy and opioids (Group L) were significantly lower than those receiving a simple opioid treatment (Group S). Therefore, it can be suggested that the analgesic effect of hyperthermia combined with opioids is superior to that of using opioids alone. Oei *et al*[15] showed

**Table 1 Comparison of baseline data between the two groups of patients, n (%)**

Baseline information	Group S (n = 35)	Group L (n = 35)	<i>t</i> / $\chi^2$	P value
Age (years)	58.54 ± 13.18	59.07 ± 13.76	0.165	0.869
Body mass index (kg/m <sup>2</sup> )	21.29 ± 1.92	21.18 ± 2.05	0.232	0.817
Sex			0.058	0.810
Male	19 (54.29)	20 (57.14)		
Female	16 (45.71)	15 (42.86)		
Tumor type			0.279	0.870
Gastric cancer	17 (48.57)	16 (45.71)		
Rectum cancer	10 (28.57)	12 (34.29)		
Colon cancer	8 (22.86)	7 (20.00)		
Tumor pathological grading			0.357	0.550
Stage III	6 (17.14)	8 (22.86)		
Stage IV	29 (82.86)	27 (77.14)		
Primary tumor diameter (cm)	5.16 ± 1.83	5.31 ± 1.97	0.330	0.742
Main distant metastatic organs				
Liver	10 (28.57)	13 (37.14)	0.583	0.445
Lungs	9 (25.71)	11 (31.43)	0.280	0.597
Peritoneum	17 (48.57)	22 (62.86)	1.447	0.229
Lymph node	15 (42.86)	13 (37.14)	0.238	0.626
Degree of cancer pain			0.245	0.621
Moderate	14 (40.00)	12 (34.29)		
Severe	21 (60.00)	23 (65.71)		

**Table 2 Comparison of cancer pain before and after analgesic treatment between the two groups of patients**

Item	Stage	Group S (n = 35)	Group L (n = 35)	<i>t</i>	P value
Average pain score (points)	Before analgesic treatment	5.79 ± 1.18	5.87 ± 1.24	0.277	0.783
	After analgesic treatment	4.56 ± 1.07 <sup>a</sup>	3.28 ± 0.85 <sup>a</sup>	5.541	< 0.001
Outbreak pain score (points)	Before analgesic treatment	7.52 ± 0.82	7.69 ± 0.93	0.334	0.739
	After analgesic treatment	6.04 ± 0.73 <sup>a</sup>	5.14 ± 0.56 <sup>a</sup>	5.787	< 0.001
Number of pain outbreaks in 24 hours (times)	Before analgesic treatment	3.35 ± 0.61	3.37 ± 0.65	0.133	0.895
	After analgesic treatment	2.38 ± 0.55 <sup>a</sup>	1.82 ± 0.49 <sup>a</sup>	4.498	< 0.001

<sup>a</sup>*P* < 0.05 vs before treatment within the group.

that the thermal effect produced by hyperthermia can dilate the blood vessels around the tumor. Consequently, we speculated that hyperthermia-induced vasodilation promotes cell membrane permeability, increases local blood flow, effectively improves local physiological metabolism and tissue hypoxia, and ultimately achieves the desired analgesic effect. Furthermore, Datta *et al*[16] revealed that hyperthermia kills tumor cells and controls the growth rate of tumor tissues through thermal effects. At the same time, it can promote the absorption of inflammatory exudate and reduce edema. From this, we speculated that hyperthermia could ultimately alleviate the cancer pain caused by tumor tissue compression, thereby relieving pain.

Kwon *et al*[17] found that heat therapy can improve immune response and activate immune cells. On the contrary, several studies have shown that oral opioid drugs can suppress the immune system function of the body[18-20]. T lymphocyte subsets (CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup>) are sensitive indicators of the immune system function. When T lymphocyte subsets and CD4<sup>+</sup>/CD8<sup>+</sup> are imbalanced they can induce immune disorders in the body[21]. The results of the present study showed that CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> after analgesic treatment in Group S were significantly lower than those

**Table 3 Comparison of immune function indicators between the two groups of patients before and after pain relief treatment**

Immune function indicators	Stage	Group S (n = 35)	Group L (n = 35)	t	P value
CD4 <sup>+</sup> (%)	Before analgesic treatment	29.67 ± 5.91	29.45 ± 5.72	0.158	0.875
	After analgesic treatment	26.05 ± 4.76 <sup>a</sup>	29.18 ± 5.64	2.509	0.014
CD8 <sup>+</sup> (%)	Before analgesic treatment	25.16 ± 4.25	25.37 ± 4.48	0.201	0.841
	After analgesic treatment	29.23 ± 3.89 <sup>a</sup>	26.28 ± 3.75	3.230	0.002
CD4 <sup>+</sup> /CD8 <sup>+</sup>	Before analgesic treatment	1.06 ± 0.23	1.04 ± 0.21	0.378	0.705
	After analgesic treatment	0.83 ± 0.17 <sup>a</sup>	0.97 ± 0.12	3.980	< 0.001

<sup>a</sup>P < 0.05 vs before treatment within the group.

**Table 4 Comparison of daily dosage and incidence of adverse reactions of opioid drugs between the two groups of patients, n (%)**

Item	Group S (n = 35)	Group L (n = 35)	t/χ <sup>2</sup>	P value
Daily dosage of opioid drugs (mg)	78.65 ± 18.92	49.74 ± 13.65	7.331	< 0.001
Adverse reactions				
Nausea and vomiting	16 (45.71)	6 (17.14)	6.629	0.010
Constipation	21 (60.00)	9 (25.71)	8.400	0.004
Dizziness and drowsiness	13 (37.14)	11 (31.43)	0.254	0.615
Delirium hallucination	3 (8.57)	2 (5.71)	0.215	0.643
Dysuria	9 (25.71)	2 (5.71)	5.285	0.022
Respiratory depression	2 (5.71)	1 (2.86)	0.348	0.555

**Table 5 Comparison of surgical palliative surgery indicators between the two groups of patients**

Item	Group S (n = 35)	Group L (n = 35)	t	P value
Surgery time (min)	184.65 ± 38.76	170.85 ± 31.69	1.631	0.108
Intraoperative blood loss (mL)	372.53 ± 79.54	343.97 ± 83.92	1.461	0.149
Surgical stress indicators				
COR (ug/L)	179.35 ± 27.86	161.43 ± 21.07	3.035	0.003
CRP (mg/L)	13.49 ± 2.17	10.51 ± 2.05	5.906	< 0.001

CRP: C-reactive protein; COR: Cortisol.

**Table 6 Comparison of postoperative recovery time between the two groups of patients**

Item	Group S (n = 35)	Group L (n = 35)	t	P value
First oral feeding time after surgery (d)	5.85 ± 1.24	4.95 ± 1.16	3.136	0.003
Postoperative hospitalization time (d)	14.49 ± 3.12	10.62 ± 2.43	5.789	< 0.001

before analgesic treatment, and CD8<sup>+</sup> was significantly increased. However, the CD4<sup>+</sup>, CD8<sup>+</sup>, and CD4<sup>+</sup>/CD8<sup>+</sup> indexes in Group L changed insignificantly compared with those before analgesic treatment, possibly because patients in Group S only used opioid drugs to control cancer pain. In order to achieve the ideal treatment effect for cancer pain in clinical practice, physicians tend to increase the dosage of opioid drugs[22], ultimately damaging patients' immune functions. Patients in Group L adopted a combination of thermal therapy and opioid analgesics for pain relief, greatly reducing the daily dosage of opioid drugs. At the same time, since thermal therapy can improve immune response and activate immune cells, this approach can better maintain the body's immune function[23]. Therefore, changes in CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> indicators before and after pain relief treatment in Group L are not. Further analysis in this study revealed

that the daily dosage of opioid drugs in Group L was significantly lower than that in Group S, supporting the above speculation. As the dosage of opioid drugs increases, the adverse reactions caused by medications will significantly increase. In this study, the incidence of adverse reactions such as nausea, vomiting, constipation, and difficulty urinating in Group L was lower than that in Group S. The combination of hyperthermia and opioid drugs reduces the dosage of opioid drugs used in patients with moderate to severe gastrointestinal cancer pain, thereby reducing or eliminating adverse reactions caused by excessive drug dosage.

Most middle and late stage gastrointestinal tumors have distant metastasis. Although palliative surgery is a commonly used method for treating middle and late stage gastrointestinal tumors[24], the trauma induced by surgery can induce varying degrees of stress reactions, subsequently causing drastic fluctuations in hemodynamic indicators. At the same time, it can also inhibit the body's immune function, suppress its anti-tumor effect, and thus undermine the effectiveness of palliative surgery. Therefore, it is essential to reduce the stress response of surgical palliative surgery. COR is a commonly used indicator for the clinical observation of stress response which can reflect immune system activity and the degree of inflammatory response[25]. As an acute protein, CRP is highly sensitive to stress response. When the body tissue is damaged, the expression level of CRP in serum rises sharply[26]. Our results showed that both COR and CRP indexes of patients in Group L were significantly lower than those in Group S on the first day after surgical palliative surgery. In addition, the postoperative recovery time of patients in group L was shorter than that of patients in group S. Consequently, it can be suggested that hyperthermia combined with opioid analgesics can reduce the stress response of surgical palliative surgery and enable patients to recover quickly after surgery. This could be because opioids weaken the immune system function through a variety of mechanisms, subsequently affecting the patient's tolerance to surgical palliative surgery and increasing the patient's surgical stress response. The thermal effect produced by hyperthermia can make the tumor tissue obtain higher temperature and longer heat storage time. Both cytotoxic and biological effects can be used to kill tumor cells, thereby reducing tumor tissue, which is conducive to the palliative surgical resection of the lesion[27]. At the same time, thermal therapy can prevent damage to the surrounding normal cells, maintaining the normal immune system function in the body. Therefore, this method not only has a minor impact on patients' palliative surgical stress, but it also reduces surgical stress response, reducing the overall postoperative recovery time.

Our study has certain limitations. First, this is a retrospective study, suggesting that there might be bias in the selection of case information. Second, this is a single-center study using a limited sample size, which may have impacted our statistical results. Therefore, prospective multicenter large sample studies may be needed to further confirm the cancer pain control effect of hyperthermia combined with opioid drugs in gastrointestinal tumors and the effect of reducing surgical palliative stress in patients.

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## CONCLUSION

The combination of hyperthermia and opioid drugs has a significantly positive effect on controlling cancer pain in patients with gastrointestinal tumors, and it can reduce the dosage of opioid drugs used by patients, thereby limiting the incidence of adverse reactions caused by drugs. At the same time, this method can also reduce the surgical stress of patients undergoing palliative surgical treatment, thereby shortening the postoperative recovery time required.

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## FOOTNOTES

**Author contributions:** Qian J and Hu CR designed the research and wrote the first manuscript; Qian J, Wu J, Zhu J, Qiu J and Wu CF contributed to conceiving the research and analyzing data; Qian J, Wu CF and Hu CR conducted the analysis and provided guidance for the research; all authors reviewed and approved the final manuscript.

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