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ORIGINAL ARTICLE

Fast-track surgery in single-hole thoracoscopic radical resection of lung cancer

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Summary

Purpose: *To explore the efficacy and safety of fast-track surgery (FTS) in the perioperative period of single-hole thoracoscopic radical resection of lung cancer.*

Methods: *The clinical data of 152 lung cancer patients undergoing single-hole thoracoscopic radical resection of lung cancer in our hospital from October 2016 to March 2019 were collected. Among them, 76 patients were treated with perioperative FTS (FTS group) following in-depth information and education, effective analgesia, early ambulation and early extubation, while the other 76 patients received conventional perioperative treatments (Control group).*

Results: *The intraoperative volumes of blood loss and fluid infusion in FTS group were smaller than those in Control group. Moreover, the mean time to postoperative drainage tube removal, time to the first postoperative ambulation and length of postoperative hospital stay in FTS group were substantially shorter than those in Control group. Moreover, the visual analog scale (VAS) scores of patients at 48 and 72 h after operation in FTS group were considerably lower than those in Control group. Besides, the total incidence rate of postoperative complications in FTS group was considerably lower than that in Control group. Compared with those before operation, all pulmonary function indicators declined substantially after operation, and the postoperative forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and maximum voluntary ventilation (MVV) in FTS group were remarkably higher than those in Control group.*

Conclusion: *FTS in the perioperative period of single-hole thoracoscopic radical resection of lung cancer can effectively accelerate the recovery of patients, alleviate their pain, shorten the length of hospital stay, reduce hospitalization expense and improve patient's satisfaction, so it is worth clinically applying.*

Key words: *fast-track surgery, single-hole thoracoscope, radical resection of lung cancer*

Introduction

Fast-track surgery (FTS), initiated by Danish surgeons Kehlet and Wilmore in 1990, refers to the concept that a series of optimized evidence-based medical measures are comprehensively applied in the perioperative period to reduce the surgical physical and psychological traumas in patients, thereby relieving the stress responses of patients to surgical traumas, facilitating the recovery of gastrointestinal function and reducing postoperative complications [1,2]. FTS is mainly composed of fast-track anesthesia, minimally invasive technique, best analgesia technique and potent postoperative care, as well as other optimized evidence-based perioperative treatments [3,4]. FTS, initially applied in cardiac surgery, has been developed to be mature and gradually applied to orthopedics, urology, gynecology and general surgery. Moreover, its safety and effectiveness have been proven by numerous studies [5-7].

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The present study, therefore, applied the FTS concept in the perioperative diagnosis and treatment schemes for the patients undergoing single-hole thoracoscopic radical resection of lung cancer and compared it with the conventional perioperative treatment measures, so as to explore the safety and efficacy of the FTS concept in the thoracic surgery.

Methods

General data

The clinical data of patients undergoing single-hole thoracoscopic radical resection of lung cancer in our hospital from October 2016 to March 2019 were collected. Inclusion criteria: 1) patients definitely diagnosed with lung cancer through preoperative fiberoptic bronchoscopy or intraoperative frozen pathology and receiving no radiotherapy or chemotherapy; 2) those who could tolerate surgery based on the physical status, with the Karnofsky Performance Score (KPS) score ≥70 points; 3) those who were able to tolerate surgery according to heart and lung functions and had basically normal liver and kidney functions; and 4) those who had no metastases or severe diseases of other organ systems as indicated by whole-body PET or CT examinations. Exclusion criteria: 1) patients with tumors which were too large or involved the vessels and trachea; 2) those with cancer cells found in the pleural effusion; 3) those who encountered conversion to thoracotomy since extensive pleural adhesions were found intraoperatively; 4) those for whom single-hole thoracoscopic surgery was converted to thoracotomy due to uncontrolled intraoperative bleeding; 5) those with distant metastases or severe anemia; 6) those complicated with severe heart, lung, liver or kidney dysfunction; 7) those complicated with other malignancies; or 8) those with poor compliance. The present study enrolled 152 patients in total, among whom there were 87 males and 65 females, aged 26-74 years old (mean 64.65±10.53). There were no statistically significant differences in the comparable baseline data such as age, gender, tumor diameter, position and stage, pathological type and ASA score between the two groups of patients ($p>0.05$) (Table 1). The study followed the Declaration of Helsinki, and patients were informed of the present study and signed the informed consent. This study was approved by the ethics committee of Liaoning Cancer Hospital & Institute.

Table 1. Demographics and general clinical data of all studied patients

Parameters	*FTS group (n=76)*	*Control group (n=76)*	*p value*
Age (years)	65.11±10.43	63.94±10.59	0.494
Gender (Male/Female)	41/35	46/30	0.512
Smoking history, cases (%)	45 (59.2)	41 (53.9)	0.624
Largest tumor diameter (cm)	3.2±1.9	2.8±1.4	0.142
Tumor location, cases (%)			0.857
Right upper lung	22 (28.9)	19 (25.0)	
Right middle lung	10 (13.2)	12 (15.8)	
Right lower lung	14 (18.4)	17 (22.4)	
Left upper lung	19 (25.0)	15 (19.7)	
Left lower lung	11 (14.5)	13 (17.1)	
Pathological type, cases (%)			0.619
Squamous cell carcinoma	31 (40.8)	28 (36.8)	
Adenocarcinoma	35 (46.1)	41 (53.9)	
Adenosquamous carcinoma	7 (9.2)	4 (5.3)	
Undifferentiated carcinoma	2 (2.6)	3 (3.9)	
Mucoepidermoid carcinoma	1 (1.3)	0 (0)	
TNM staging, n (%)			0.284
I	28 (36.8)	31 (40.8)	
II	37 (48.7)	40 (52.6)	
IIIa	11 (14.5)	5 (6.6)	
ASA grade, n (%)			0.313
1	25 (32.9)	31 (40.8)	
2	51 (67.1)	45 (59.2)	

FTS: Fast track surgery; TNM: Tumor, lymph node, metastasis; ASA: American Society of Anesthesiologists

Surgical procedures

Perioperative FTS was conducted in the FTS group as follows: Preoperative health education and mental support were first completed. Thoracic surgery causes large traumas and intense stress responses, thereby increasing the risk of complications, and reducing the stress responses of patients can promote their recovery, which is the core of the FTS concept. Then, the medical staff actively communicated with patients to relieve their mental burden. Before operation, the patients were informed of the surgical methods, incision size and the purpose of postoperative chest tube indwelling, and the advantages of single-hole thoracoscopic surgery were stressed. Preoperative preparations: Physical exercise and respiratory function exercise were performed using breathing exerciser or by blowing a balloon. Besides, the malnourished patients were given appropriate nutritional support, and all the patients were fasted for food 6 h before operation, allowed to drink 300-500 mL of water 4 h before operation and intravenously dripped with antibiotics 30 min before operation. Intraoperative treatments: The patients were kept warm during routine disinfection and generally anesthetized using drugs with a short half-life. The incision was protected by an incision protection sleeve, and the operations should be gentle to avoid excessively pulling and squeezing lung tissues. Moreover, restricted fluid infusion was conducted, with the fluid volume <1,000 mL, and vasoactive drugs were used to raise the blood pressure. Finally, a pleural drainage catheter was indwelled and led out from the incision. Postoperative treatments: On the day of operation, the patients were instructed to do sit-ups on the bed for 2-3 times. Additionally, they were encouraged to actively move their lower limbs or their family members massaged the patients' lower limb muscles, combined with the adjutant pneumatic pump therapy, to prevent deep-vein thrombosis. At 6 h after operation, the patients were given water and liquid food. On 1 day after operation, the patients ate normally eat in the morning, and they were encouraged to get off bed and ambulate for 4-6 times (about 10 min/time). The ambulation time was extended 2 days after operation. Additionally, the patient-controlled analgesia pump was applied to ease pain, and the patients were encouraged to cough and expectorate. Extubation indications: The chest tube was squeezed once every 30 min to avoid blocking tube opening and ensure the smooth drainage of intrapleural fluid, thereby accelerating the recovery of pulmonary function. Finally, the tube was removed when there was no air leak of the closed thoracic drainage bottle, and no bloody, chylous or purulent pleural effusion, X-ray chest imaging indicated favorable lung recruitment, with the 24 h-pleural drainage volume <200 mL, and the postoperative daily intravenous fluid infusion was controlled to be <800 mL.

Conventional perioperative treatment was adopted in the Control group: On admission, the patients and their family members were informed of the preoperative smoking cessation and breathing exercise. On day 1 before operation, the patients and their families were routinely informed of the surgical methods, surgical incision size, surgical risk and perioperative precautions, and on the evening of that day, the patients ate liquid food. At 10 h before operation, the patients were deprived of food and water. Intraoperatively, blood volume was routinely enlarged to increase the blood pressure. At 24 h after operation, the patients were given food and water, and under the routine monitoring of vital signs, they were intramuscularly injected with analgesics and provided with rehabilitation guidance. Extubation indications: 1) there was no air leak of the closed thoracic drainage bottle; 2) the pleural effusion was not bloody, chylous or purulent; 3) Chest X-ray imaging indicated complete lung recruitment; and 4) the 24 h-pleural drainage volume was <100 mL.

Observation indicators

The surgical conditions of patients, including operation time, volume of intraoperative blood loss and volume of intraoperative fluid infusion, were recorded. Postoperative recovery was assessed based on the time to the first postoperative ambulation, time to postoperative drainage tube removal and visual analogue scale (VAS) score in the morning at 24, 48 and 72 h after operation. The pain was scored according to the following criteria: no pain is given 0 point, occasionally mild pain 1-2 points, mild pain 3-4 points, occasionally obvious but tolerable pain 5-6 points, frequently obvious and intolerable pain 7-8 points and severe pain 9-10 points. Moreover, the levels of C-reactive protein (CRP), interleukin (IL)-6 and tumor necrosis factor alpha (TNF-α)-1 day before operation and 7 days after operation were compared between the two groups of patients. The length of postoperative hospital stay, hospitalization expense and patient's satisfaction score were compared between the two groups of patients. The pulmonary function indicators vital capacity (VC), forced expiratory volume in the first second (FEV1) and maximum voluntary ventilation (MVV) were also compared between the two groups of patients. Besides, the incidence of postoperative complications was recorded in the two groups of patients.

Discharge criteria: After drainage tube removal, the wound healed well, the body temperature was not high, and the chest pain was not obvious or could be controlled by orally taking a few analgesics. Moreover, the re-examination of chest X-ray indicated no more than 30% pneumothorax, no obvious pleural effusion and no chest infections, and the patients had no special discomfort during ambulation.

Statistics

SPSS 22.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. Measurement data were presented as mean ± standard deviation (x±s) and the intergroup comparisons were made using pairwise t-test. Enumeration data were expressed as ratio (%), and x^2 test was performed for intergroup comparisons. The survival curves were plotted using the Kaplan-Meier method and log-rank test was utilized to compare the survival rates between the two groups. P<0.05 suggested that the differences were statistically significant.

Results

Comparisons of surgical indicators between the two groups of patients

There was no statistically significant difference in the specific surgical method between FTS group (n=76) and Control group (n=76) (p=0.527) (Table 2). Moreover, the operation time of patients was 145.8±40.4 min in the FTS group and 139.5±53.6 min in the Control group, showing no statistically significant difference (p=0.415). The FTS group exhibited substantially smaller volumes of intra-operative blood loss and fluid infusion than the Control group (113.3±22.7 mL *vs.* 120.6±20.8) mL, p=0.041, and 887.9±176.5 mL *vs.* 1031.1±200.7 mL, p=0.004) (Table 2).

Comparison of postoperative recovery between the two groups of patients

Abdominal drainage tubes were indwelled postoperatively in 44 out of 76 patients in the FTS group, and in 55 out of 76 patients in the Control group, and there was a statistically significant difference in the mean time to drainage tube removal between the two groups (3.2±1.2 d *vs.* 5.8±1.5 d, p<0.001). In the FTS group, 25 patients went out of the bed and ambulated one day after operation, 33 patients on day 2 after operation and 18 patients on day 3 after operation and later. In the Control group, there were 13 cases of ambulation one day after operation, 29 cases on day 2 after operation and 34 cases on.day 3 after operation and later. There was a statistically significant difference in the mean time to ambulation between the two groups (1.6±0.5 d *vs.* 2.7±0.7, d;p<0.001). The length of postoperative hospital stay in the FTS group was considerably shorter than that in the Control group (p<0.001), and the total hospitalization expense in the FTS group was notably less than that in the Control group (p<0.001). Moreover, the FTS group showed a considerably higher patient's satisfaction score than the Control group (p=0.019). The mean visual analog scale (VAS) scores of patients at 24, 48 and 72 h after operation were 5.58±0.87 points, 4.84±0.64 points and 4.22±0.59 points, respectively, in the FTS group, and 5.75±0.75 points, 5.13±0.68 points and 4.66±0.61 points, respectively, in the Control group. It can be seen that the VAS scores at 48 and 72 h after operation in the FTS group were considerably lower than in the Control group (p=0.018, p=0.009) (Table 2 and Figure 1).

Comparisons of postoperative complications between the two groups of patients

After operation, the two groups of patients had the main complications, including postoperative

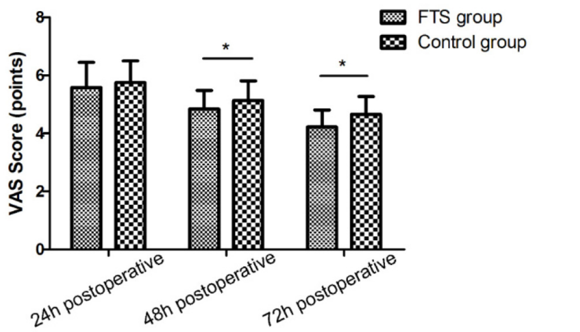

Figure 1. Comparison of VAS score of patients in the two groups. There was no significant difference between 24 hours postoperative VAS scores of patients in FTS group and Control group (p=0.199). Both 48 hours and 72 hours postoperative VAS scores of patients in FTS group were significantly lower than that of Control group (p=0.018, p=0.009, *p<0.05).

Table 2. Comparison of parameters related to surgery of the studied patients in two different groups

Parameters	*FTS group (n=76)*	*Control group (n=76)*	*p value*
Surgical procedure			0.527
Wedge Resection of lung	35 (46.1%)	31 (40.8%)	
Segmental Resection of Lung	22 (28.9%)	24 (31.6%)	
Lobectomy of lung	19 (25.0%)	21 (27.6%)	
Operation time (min)	145.8±40.4	139.5±53.6	0.415
Blood loss (mL)	113.3±22.7	120.6±20.8	0.041
Intraoperative fluid input volume (mL)	887.9±176.5	1031.1±200.7	0.004
Postoperative drainage tube removal time (d)	3.2±1.2	5.8±1.5	0.001
Postoperative in-hospital time (d)	5.2±0.8	7.2±1.1	0.001
Postoperative off-bed activity time (d)	1.6±0.5	2.7±0.7	0.001
Hospitalization expense (10,000 yuan)	3.1±0.6	3.8±0.7	0.001
Patient satisfaction score (points)	8.4±1.3	7.9±1.1	0.019

FTS: Fast track surgery

incision infection, atelectasis, pulmonary air leakage, pulmonary infection, pleural effusion, respiratory failure, arrhythmia and thrombosis. Moreover, the incidence rate of pleural effusion in the FTS group was considerably lower than that in the Control group (2.6% *vs.* 10.5%, p=0.034), and the total incidence rate of postoperative complications in the FTS group was considerably lower than that in the Control group as well [17.1% (13/76) *vs.* 39.5% (30/76), p=0.004] (Table 3).

Comparison of improvement of pulmonary function between the two groups of patients

There were no statistically significant differences in the pulmonary function indicators forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and maximum voluntary ventilation (MVV) between the two groups before operation (p>0.05). Compared with those before operation, all pulmonary function indicators declined substantially after operation (p<0.05), and the postoperative FVC, FEV1 and MVV in the FTS group were remarkably higher than those in the Control group (p=0.038, p=0.03 and p=0.015) (Table 4).

Comparisons of serum CRP, IL-6 and TNF-α after operation between the two groups of patients

The mean levels of serum CRP on day 1 before operation and on day 7 after operation were 16.9±3.7 and 23.4±12.7 mg/L, respectively in the FTS group, and 17.8±4.7 mg/L and 28.4±13.6 mg/L, respectively, in the Control group. The mean levels of serum IL-6 on day 1 before operation and on day 7 after operation were 70.20±8.98 ng/mL and 127.72±18.28 ng/mL, respectively, in the FTS group, and 71.17±8.62 mg/L and 141.05±20.46 ng/mL, respectively, in the Control group. Moreover, the levels of serum TNF-α on day 1 before operation and on day 7 after operation were 0.83±0.46 pg/mL and 1.88±0.68 pg/mL, respectively, in the FTS group, and 0.87±0.43 pg/mL and 2.13±0.59 pg/mL, respectively, in the Control group. There were no statistically significant differences in the levels of serum CRP, IL-6 and TNF-α on day 1 before operation between the two groups (p=0.192, p=0.498 and p=0.581), but their levels on day 7 after operation in the FTS group were prominently lower than those in the Control group (p=0.033, p<0.001 and p=0.017) (Figure 2).

Table 3. Comparison of postoperative complications of the studied patients in two different groups

Complications	*FTS group (n=76) n (%)*	*Control group (n=76) n (%)*	*p value*
Pulmonary atelectasis	2 (2.6)	3 (3.9)	0.743
Pulmonary infection	3 (3.9)	5 (6.6)	0.533
Pulmonary air leakage	0 (0)	2 (2.6)	0.497
Pleural effusion	2 (2.6)	8 (10.5)	0.034
Respiratory failure	1 (1.3)	1 (1.3)	1.000
Arrhythmia	4 (5.3)	7 (9.2)	0.368
Incision infection	1 (1.3)	2 (2.6)	0.702
Thrombosis	0 (0)	1 (1.3)	0.648

FTS: Fast track surgery

Table 4. Comparison of preoperative and postoperative pulmonary function parameters of the studied patients in two different groups

Parameters	*FTS group (n=76)*	*Control group (n=76)*	*p value*
FVC (L)			
Preoperative	2.65±0.31	2.69±0.28	0.405
Postoperative	2.24±0.25	2.16±0.22	0.038
FEV1 (L)			
Preoperative	2.02±0.18	2.06±0.21	0.209
Postoperative	1.86±0.15	1.78±0.17	0.030
MVV (L/min)			
Preoperative	77.1±5.61	78.5±5.47	0.121
Postoperative	66.4±4.34	64.7±4.21	0.015

FTS: Fast track surgery; FVC: Forced vital capacity; FEV: Forced Expiratory Volume; MVV: Maximum Ventilatory Volume

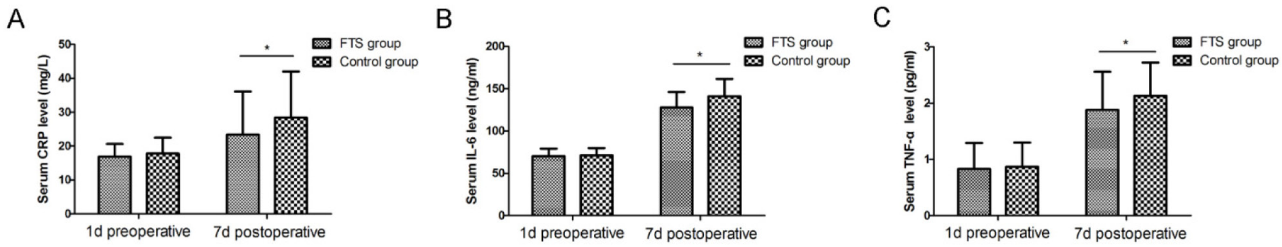

Figure 2. Comparison of serum CRP, IL-6 and TNF-α levels of patients in the two groups. Preoperative CRP **(A)**, IL-6 **(B)** and TNF-α **(C)** levels of patients had no significant difference between FTS group and Control group (p=0.192, p=0.498, p=0.581). Postoperative serum CRP **(A)**, IL-6 **(B)** and TNF-α **(C)** levels of patients in both groups significantly increased after surgery (p<0.05). The posttreatment CRP **(A)**, IL-6 **(B)** and TNF-α **(C)** levels of patients in FTS group were significantly lower than that of Control group (p=0.033, p<0.001, p=0.017, *p<0.05).

Discussion

The concept of FTS is a cutting-edge technique and an idea that integrates multidisciplinary collaborations involving anesthesia, nursing and surgery, with the core of optimizing the perioperative treatment and nursing measures and reducing complications and stress responses and the premise of accelerating recovery [8]. According to the results of numerous randomized controlled studies, the length of postoperative hospital stay is 7-11 days and the incidence rate of complications is 10-25% in the lung cancer patients receiving conventional perioperative treatments. Moreover, the thoracoscopic surgery for lung cancer can shorten the length of hospital stay to 3-7 days. In recent years, some European countries and America have been strongly promoting the concept of FTS that has a profound effect in promoting the restoration of pulmonary function and accelerating the postoperative recovery of patients [9-12].

At present, multiple medical centers have performed 3-hole and single-hole thoracoscopic resection of lung lobes or lung segments, radical resection of lung cancer and lymph node dissection and found that single-hole thoracoscopic surgery causes small traumas, with rapid postoperative recovery of patients. Single-hole thoracoscopic surgery has the advantages of small incision, mild pain, few impacts on patients' psychology and physiology, which coincide with FTS [13,14]. Since small surgical traumas and shorter operation time ensure mild postoperative stress responses, the patients may rapidly recover after operation only when the surgery-induced stress responses in organisms are attenuated to the largest extent [15]. In this study, the perioperative treatment was altered under the guidance of FTS combined with the advantages of single-hole thoracoscopic surgery in the FTS group. It was found that the indicators volume of intraoperative blood loss, volume of intraoperative fluid infusion, postoperative pain, complications, chest tube indwelling time and length of hospital stay were superior to those in the Control group, suggesting that FTS is safe and feasible in single-hole thoracoscopic radical resection of lung cancer, and it accelerates the recovery and reduces complications.

The volume of restricted fluid infusion and postoperative pain are independent risk factors for the incidence of complications after radical resection of lung cancer. A study demonstrated that after lobectomy or segmentectomy, the pulmonary volume is reduced, so large amounts of normal saline are infused intraoperatively and postoperatively to maintain an ideal blood pressure and constant organ perfusion. However, excessive circulating blood volume causes fluid extravasation, leading to postoperative water and sodium retention in organisms, increases cardiopulmonary vascular load to induce pulmonary edema and complications such as postoperative pulmonary infection, arrhythmia and prolonged intestinal paralysis, and prolongs the postoperative recovery of gastrointestinal function, thereby extending the time to eating and recovery of patients [16]. Moreover, it is helpful to decrease the volume of intraoperative fluid infusion to be no more than 1,000 mL for reducing the incidence rate of pulmonary edema-induced pulmonary infections. The FTS concept advocates the restricted infusion. Hence, when hypotension occurs intraoperatively and postoperatively, with effective circulating blood volume ensured, vasoactive drugs and colloid solution are preferentially used to increase blood pressure, thereby avoiding pulmonary edema and pulmonary infection, thus improving the postoperative blood-oxygen exchange and oxygen saturation and diffusion and reducing pleural effusion [17,18].

"Effective analgesia" is an important component of the FTS concept. Minimally invasive single-hole thoracoscopic surgery greatly relieves postoperative pain, effectively maintains the integrity of the chest wall, and improves postoperative pulmonary function [19]. According to the results of the present study, the FTS group had a notably lower pain score than the Control group within 3 days after operation. Effective pain controlling is the foundation of postoperative cough, expectoration and ambulation, while early pulmonary exercise is the key to reducing postoperative pulmonary complications. The application of FTS lowered the incidence rate of postoperative complications, instead of increasing it. Moreover, postoperative analgesia with patient-controlled analgesia pump alleviates pain, thereby helping with cough, expectoration and early ambulation, and reducing the incidence rates of pulmonary infection and atelectasis [20]. Meanwhile, bed rest changes the hydrostatic pressure gradient, expands the range of lung ptosis, enlarges the pulmonary congestion volume, and disorders the ventilation-blood flow ratio, thus easily inducing pulmonary edema and ultimately leading to pulmonary complications. The early ambulation and pulmonary function exercise of patients help accelerate the recovery of function and reduce the risk of bed rest-induced pulmonary complications [21]. Therefore, the application of FTS concept obviously alleviates the postoperative pain stimulation and helps accelerate the postoperative recovery.

Conclusion

FTS in the perioperative period of single-hole thoracoscopic radical resection of lung cancer can effectively accelerate the recovery of patients, alleviate their pain, shorten the length of hospital stay, reduce hospitalization expense and improve patient's satisfaction, so it is worth of clinical application.

Conflict of interests

The authors declare no conflict of interests.

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