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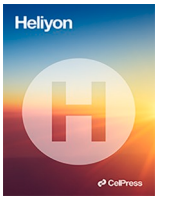

Research article

Comparative study of acute and chronic pain after inflatable videoasisted MediastinoscopicTranshiatal esophagectomy and minimally invasive McKeown Esophagectomy:A propensity score matching analysis

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ABSTRACT

Objective: The short-term quality of life of patients can be enhanced by performing Inflatable Video-Assisted Mediastinoscopic Transhiatal Esophagectomy (IVMTE). Nevertheless, there is limited research on how it impacts postoperative acute and chronic pain in individuals diagnosed with esophageal cancer.Hence, this research aimed to examine the impact of IVMTE and minimally invasive Mckeown esophagectomy (MIME) on the occurrence of acute and chronic pain following surgery in individuals diagnosed with esophageal cancer.

Methods: A retrospective, propensity score matching analysis was adopted. In total, 133 patients with esophageal cancer who underwent IVMTE and MIME between January 2020 and December 2021 were part of the study. Among them, 38 patients underwent IVMTE and 95 patients underwent MIME. Following the propensity score matching analysis, 36 patients were included in each group. Patients' postoperative pain was evaluated using the numerical rating scale (NRS).

Results: The IVMTE group (Group A) had significantly reduced operation time and intraoperative blood loss compared to the MIME group (Group B) ($P < 0.05$). NRS scores on the 1st, 2nd, 3rd, and 7th days after surgery, as well as on the 3rd and 6th months post-surgery, were notably reduced in the IVMTE group (Group A) compared to the MIME group (Group B) ($P < 0.05$). Univariate and multivariate analysis showed that chronic pain occurred postoperative 3rd months was related to the operation methods ($P < 0.05$). Univariate analysis showed that chronic pain occurred postoperative 6th months was related to the operation time, postoperative 14th days NRS scores and operation methods ($P < 0.05$). Multivariate analysis showed that chronic pain occurred postoperative 6th months was related to the operation methods ($P < 0.05$).

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Conclusion: The results showed that the operation methods were the main risk factors for post-operative chronic pain. The compared with MIME, IVMTE can further reduce the acute and chronic pain of patients with esophageal cancer.

Abbreviation

IVMTE	Inflatable videoasisted mediastinoscopic transhiatal esophagectomy
MIME	Minimally invasive Mckeown esophagectomy
NRS	Numerical rating scale
MIE	Minimally invasive esophagectomy
CT	Computed tomography
PET-CT	Positron emission tomography-computed tomography
ASA	American society of Aneshesiologist
AJCC	The American Joint Committee on Cancer
TNM	Tumor node metastasis

1. Introduction

Esophageal cancer is one of the most invasive malignant tumors of digestive tract. Of all cancers, its morbidity ranks eighth and mortality ranks sixth [1,2]. Surgery-based comprehensive treatment is still the main treatment for patients with resectable esophageal cancer [3–5]. With the development of endoscopic technology, minimally invasive esophagectomy(MIE) has gradually replaced the traditional open surgery as a mainstream operation. Studies have shown that the perioperative effect of MIE is better than that of open esophagectomy [6,7]. According to the method used, it can be divided into minimally invasive McKeown esophagectomy (MIME), minimally invasive Ivor-Lewis esophagectomy, minimally invasive Sweet esophagectomy, and inflatable videoasisted mediastinoscopic transhiatal esophagectomy (IVMTE) [8–11]. Traditional open esophagectomy results in large trauma, slow recovery, and poor short-term and long-term quality of life. MIE retains the integrity of the chest and abdominal wall, and the operation is more accurate, significantly reducing the incidence of surgical trauma and postoperative complications [12–14]. With the continuous development of endoscopic technology, mediastinoscopy combined with laparoscopic surgery has become a new approach for esophageal cancer surgery. This operation avoids intercostal incision and further reduces chest wall trauma, especially for early esophageal cancer patients with poor cardiopulmonary function [15,16].

Postoperative pain is one of the most common symptoms after thoracic surgery. It not only increases the incidence of postoperative complications, but also has a significant negative effect on the psychology and postoperative recovery of patients [17,18]. Recent research has indicated that there is no notable disparity in safety and efficacy between IVMTE and MIME, with the former even surpassing the latter in terms of operation duration [19,20]. However, there are few comparative studies on acute and chronic postoperative pain between the two types of surgery. In 2007, our hospital began to perform MIE for esophageal cancer, including MIME, minimally invasive Ivor-Lewis surgery and minimally invasive Sweet surgery. In 2017, IVMTE will be implemented. This method avoids chest wall incision and postoperative indwelling chest tube, and theoretically further reduces the postoperative pain of patients [21,22]. A retrospective analysis using propensity score matching was conducted on clinical data from patients who received IVMTE or MIME at the First Affiliated Hospital of the University of Science and Technology of China between January 2020 and December 2021. The study compared the rates of acute and chronic postoperative pain in both groups and assessed the potential of IVMTE in reducing postoperative pain incidence.

2. Materials and methods

2.1. Object of study

A study was conducted retrospectively, using propensity score matching, on individuals who received minimally invasive esophagectomy at the thoracic surgery unit of the First Affiliated Hospital of University of Science and Technology of China, spanning from January 2020 to December 2021. The inclusion criteria were as follows: (1) esophageal cancer; (2) acceptance of IVMTE or MIME; and (3) normal mental state, able to understand and cooperate with pain assessment. The exclusion criteria were as follows: (1) history of chronic pain before operation; (2) preoperative radiotherapy and chemotherapy; (3) serious postoperative complications, such as anastomotic fistula, or inability to cooperate with pain assessment and follow-up after discharge; and (4) chronic infection, disease recurrence or reoperation after initial surgery.

After applying the criteria for inclusion and exclusion, a total of 133 patients were selected for the study, with 38 patients assigned to Group A for IVMTE and 95 patients assigned to Group B for MIME. Following the propensity score matching analysis, 36 patients were included in each group.

Various tests were conducted on all patients including blood routine, biochemical analysis, coagulation studies, immunohistochemistry, esophageal barium swallow, electronic gastroscopy, ultrasound endoscopy, electrocardiogram, echocardiography, pulmonary function testing, chest and upper abdominal computed tomography (CT) scan, as well as neck and abdominal ultrasound to assess tumor size, invasion depth, tissue relationships, lymph node status, and rule out distant metastasis and significant esophageal tumor invasion. Certain individuals received positron emission tomography-computed tomography (PET-CT) scans for staging before surgery.

Tumor staging utilized the eighth edition tumor node metastasis (TNM) classification from the American Joint Committee on Cancer (AJCC). Prior to the surgery, each patient was assessed based on the classification criteria set by the American Society of Anesthesiologists (ASA). The Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China approved this study under the reference number (NO.2022-RE-145).

2.2. Surgical procedures

IVMTE: The individual was sedated using a single-lumen endotracheal tube and positioned on their back. The shoulder and back were lifted, while the head was tilted to the right to completely reveal the left side of the neck. A 3 cm long cut was created on the inner side of the left sternocleidomastoid muscle, layer by layer, to separate the muscle group, release the cervical esophagus, and identify the location for safeguarding the recurrent laryngeal nerve. To create a sealed space, the protective sleeve for the incision and gloves were used. After the inflation pressure in the mediastinum was 8 mmHg and the flow 5L-6/min, the operating instrument was placed. The esophagus was dissected downwards along the left side of the cervical esophagus following the sequence of 'left, front, right, back' until reaching the inferior carina or the inferior pulmonary ligament level. The lymph nodes surrounding the recurrent laryngeal nerve, esophagus, and inferior carina were then cleared. During the procedure, care was taken to safeguard the recurrent laryngeal nerve, azygos vein arch, and thoracic duct. Abdominal operation and digestive tract reconstruction were the same as in the MIME procedure.

MIME: The patient laid on their left side and underwent left single-lung ventilation. The primary surgical incision was made with a length of 2 cm in the 4th intercostal space on the right side of the chest near the front armpit line, while a secondary incision of 1 cm was created in the 7th intercostal space at the midline of the armpit, and an additional incision of 1.5 cm was made in the 8th intercostal space between the back armpit line and the line of the shoulder blade for auxiliary procedures. The azygos vein was tied off using hemoblock and subsequently cut. The thoracic esophagus was dissociated with an ultrasonic scalpel and electric hook. Finally, the lymph nodes near the recurrent laryngeal nerve, near the esophagus and under the carina were routinely explored. The suspected enlarged lymph nodes were cleaned during the operation, and the lymph nodes without obvious enlargement were sampled. After the chest operation, the patient was moved to the supine position. The abdominal surgery was identical to that performed on the mediastinoscopy group. Following the insertion of the stomach tube, the tissue was incised along the inner border of the left cervical sternocleidomastoid muscle to release the cervical esophagus. The surgeon brought the esophagus up through the neck incision and connected it to the stomach tube using a circular stapler. Following the connection of blood vessels, the stomach tube and duodenal feeding tube were inserted via the incision in the abdomen, and both the abdominal and neck incisions were then sealed.

2.3. Observation indicators

Patients' postoperative pain was evaluated using the numerical rating scale (NRS). Based on the evaluation findings, the individuals were categorized into four levels: absence of discomfort (NRS 0), slight discomfort (NRS 1–3), moderate discomfort (NRS 4–6), and intense discomfort (NRS 7–10). A nurse and a doctor assessed the patient's pain level in person twice daily following the surgery. The average pain score per day was used as the daily pain intensity index until discharge. Patients were contacted by phone 3 and 6 months post-surgery to document the specific details of pain, including its location, severity (NRS score), and characteristics. Age, sex, tumor location, TNM stage, degree of tumor differentiation, ASA classification, preoperative complications, perioperative information, and the postoperative 1st, 2nd, 3rd, 7th and 14th days NRS scores and the postoperative 3rd and 6th months NRS scores were observed and recorded.

2.4. Statistical analyses

The data were analyzed by SPSS26.0 statistical software, and the patients' age, sex, tumor location, TNM stage, Degree of tumor differentiation, ASA classification and Preoperative complications were calculated by using SPSS26.0 statistical software. The items with the most similar trend score in both sets were paired based on a ratio of 1:1, with a threshold value of 0.02. Data following a normal distribution are presented as $\bar{X} \pm S$, and the average values of the two groups were compared using a *t*-test. The counting data are expressed as frequency and percentage, and the differences between groups were compared by $\chi 2$ test. Pearson analysis was used to compare the correlation between the degree of acute and chronic pain of postoperative patients. Logistic regression was used to analyze the factors that influence acute and chronic pain. There was a statistically significant variance ($P < 0.05$).

3. Result

3.1. Comparison of clinicopathological data

Before the propensity matching analysis, there was no significant difference in age, sex, tumor location, TNM stage, degree of tumor

differentiation and preoperative complications between the two groups(P > 0.05). The ASA score was significantly higher in IVMTE group than in MIME group (P = 0.042). After propensity matching analysis, 36 patients were included in each group. There was no significant difference in age, sex, tumor location, TNM stage, degree of tumor differentiation, ASA classification and preoperative complications between the two groups(P > 0.05) (Table 1).

3.2. Comparison of perioperative data and postoperative pain NRS scores

There was no significant difference in postoperative hospital stay between the two groups (P = 0.987), but the operation time was shorter, and the blood loss was less in IVMTE group than in MIME group(P = 0.008 and P = 0.006)(Table 2).

The postoperative 1st, 2nd, 3rd and 7th days NRS scores in IVMTE group were significantly lower than those in MIME group (P < 0.05, Table 2). There was no significant difference in postoperative 14th NRS scores between the two groups (P = 0.133). The incidence of chronic pain in the IVMTE group was lower than that in the MIME group at postoperative 3rd and 6th months, and the difference was statistically significant(P = 0.018 and P = 0.002)(Table 2).

3.3. Univariate and multivariate analysis of influencing factors of postoperative chronic pain

Univariate analysis of the clinical data showed that operation methods were significantly correlated with the chronic pain occurred postoperative 3rd months (P = 0.018) (Table 3). Univariate analysis of the clinical data showed that operation time, postoperative 14th days NRS scores and operation methods were significantly correlated with the chronic pain occurred postoperative 3rd months (P = 0.017, P = 0.034 and P = 0.002) (Table 3). Multivariate analysis of the clinical data showed that operation methods were significantly correlated with the chronic pain occurred postoperative 3rd and 6th months (P = 0.019 and P = 0.010) (Table 4).

4. Discussion

The most common surgical approach for operable esophageal cancer involves a combination of thoracoscopy and laparoscopic resection. Compared with traditional open surgery, MIE protects the integrity of the thoracoabdominal wall, with more delicate anatomy, less trauma and faster recovery []. However, there are still several small incisions on the chest wall, and the intercostal nerve is damaged to a certain extent. Most patients will still experience a certain degree of acute pain after surgery, and some patients even experience chronic pain. IVMTE has no chest incision or postoperative indwelling chest tube, completely avoiding injury to the intercostal nerve. Theoretically, it has the potential to further alleviate the severe and long-lasting pain experienced by individuals with esophageal cancer [,23,24]. Research indicated a notable decrease in acute and chronic pain among patients who received IVMTE compared to those who received MIME, highlighting the benefits of IVMTE in managing postoperative pain.

Postoperative pain after thoracic surgery is a mixed pain that mainly includes neuropathic and myofascial pain. Postoperative pain leads to the obstruction of cough and sputum excretion and increases the incidence of postoperative pulmonary complications. At the same time, postoperative pain has a serious negative impact on the patient's psychology, which further affects the patient's postoperative recovery. Hence, the primary concern of thoracic surgeons is determining the optimal surgical approach for alleviating acute

Table 1
Clinical case characteristics of the patient.

	Before PSM ($n = 133$)			After PSM ($n = 72$)		
	Group A ($n = 38$)	Group B ($n = 95$)	p	Group A ($n = 36$)	Group B ($n = 36$)	p
Sex			0.404			0.789
Male	27	74		26	27	
Female	11	21		10	9	
Age(year)	68.87 ± 8.86	67.03 ± 8.64	0.274	68.47 ± 8.83	70.06 ± 9.45	0.465
Tumor location			0.488			0.857
Upper	4	18		4	4	
Middle	25	28		24	22	
Lower	9	19		8	10	
TNM stage			0.973			0.615
I	21	51		20	17	
II	12	32		11	15	
III	5	12		5	4	
Degree of tumor differentiation			0.669			0.685
High	7	21		7	10	
Middle	19	51		18	17	
Low	12	23		11	9	
ASA classification			0.042			0.635
II	15	56		15	17	
III	23	39		21	19	
Preoperative complications			0.869			0.814
Yes	19	46		18	17	
No	19	49		18	19	

Table 2
Comparison of intraoperative and postoperative pain scores between the two groups.

	Group A(n = 36)	Group B (n = 36)	*p*
Operation time	221.72 ± 47.09	254.00 ± 52.42	0.008
Intraoperative blood loss	74.17 ± 29.94	116.67 ± 83.50	0.006
Postoperative hospital stay	17.28 ± 7.77	17.31 ± 6.42	0.987
Acute pain (NRS)			
Postoperative 1st day	4.86 ± 1.55	6.03 ± 1.40	0.001
Postoperative 2nd day	3.00 ± 1.33	4.75 ± 1.78	0.001
Postoperative 3rd day	2.50 ± 1.56	3.28 ± 1.09	0.016
Postoperative 7th day	2.06 ± 1.29	2.89 ± 0.95	0.003
Postoperative 14th day	1.69 ± 1.04	2.03 ± 0.81	0.133
Chronic pain (NRS)			
Postoperative 3rd month			0.018
No	21 (58.33 %)	11 (30.56 %)	
Yes	15 (41.67 %)	25 (69.44 %)	
Postoperative 6th month			0.002
No	27 (75.0 %)	14(38.89 %)	
Yes	9(25.0 %)	22(61.11 %)	

Table 3
Analysis of related factors influencing postoperative chronic pain.

	Chronic pain (3 months)			Chronic pain (6 months)		
	NO	YES	*p*	NO	YES	*p*
Age(year)	67.91 ± 9.14	70.35 ± 9.06	0.261	67.71 ± 8.951	71.32 ± 9.057	0.096
Operation time	231.69 ± 49.18	242.8 ± 54.38	0.372	225.24 ± 49.124	254.55 ± 51.915	0.017
Intraoperative blood loss	97.66 ± 89.13	93.63 ± 39.67	0.813	91.34 ± 80.584	100.81 ± 39.414	0.515
Postoperative 1st day	5.47 ± 1.83	5.43 ± 1.37	0.911	5.41 ± 1.688	5.48 ± 1.458	0.856
Postoperative 2nd day	3.53 ± 1.87	4.15 ± 1.70	0.147	3.68 ± 1.781	4.13 ± 1.803	0.299
Postoperative 3rd day	2.66 ± 1.49	3.08 ± 1.28	0.206	2.71 ± 1.537	3.13 ± 1.147	0.205
Postoperative 7th day	2.31 ± 1.23	2.6 ± 1.17	0.315	2.32 ± 1.213	2.68 ± 1.166	0.209
Postoperative 14th day	1.63 ± 0.83	2.05 ± 0.98	0.056	1.66 ± 0.794	2.13 ± 1.056	0.034
Sex			0.403			0.658
Male	22(68.75 %)	31(77.50 %)		31(75.61 %)	22(70.97 %)	
Female	10(31.25 %)	9(22.50 %)		10(24.39 %)	9(29.03 %)	
Operation methods			0.018			0.002
IVMTS	21(65.63 %)	15(37.50 %)		27(65.85 %)	9(29.03 %)	
MIME	11(34.37 %)	25(62.50 %)		14(34.15 %)	22(70.97 %)	
Tumor location			0.943			0.445
Upper	4(12.50 %)	4(10.00 %)		6(14.63 %)	2(6.45 %)	
Middle	20(62.50 %)	26(65.00 %)		24(58.54 %)	22(70.97 %)	
Lower	8(25.00 %)	10(25.00 %)		11(26.83 %)	7(22.58 %)	
TNM stage			0.278			0.068
I	19(59.38 %)	18(45.00 %)		24(58.54 %)	13(41.94 %)	
II	11(34.37 %)	15(37.50 %)		15(36.59 %)	11(35.48 %)	
III	2(6.25 %)	7(17.50 %)		2(4.87 %)	7(22.58 %)	

Table 4
Logistic regression analysis of influencing factors of postoperative chronic pain.

	β	$S_{\bar{x}}$	*Wald*	*OR (95 % CI)*	*p*
Chronic pain (3 months)					
Intraoperative blood loss	−0.005	0.005	1.207	0.995 (0.986–1.004)	0.272
Operation time	−0.002	0.005	0.080	0.998 (0.988–1.009)	0.777
Postoperative 14th day	0.471	0.294	2.560	1.601 (0.900–2.849)	0.110
Operation methods	−1.308	0.570	5.267	0.270 (0.088–0.826)	0.022
Chronic pain (6 months)					
Intraoperative blood loss	−0.002	0.004	0.266	0.998 (0.990–1.006)	0.453
Operation time	0.007	0.006	1.422	1.007 (0.996–1.018)	0.233
Postoperative 14th day	0.415	0.300	1.920	1.515 (0.842–2.726)	0.166
Operation methods	−1.405	0.571	6.043	0.245 (0.080–0.752)	0.014

and chronic pain in patients suffering from esophageal cancer.

The acute pain of postoperative patients with esophageal cancer is often severe, characterized by pain relief during bed rest and peak pain during cough, and increases the incidence of postoperative complications and length of postoperative hospital stay. The

study findings indicate that pain occurrence in the IVMTE group was notably lower on the first and second days post-operation compared to the MIME group. Therefore, inflatable mediastinoscopy has more advantages in terms of the pain score on the 1st and 2nd days after the operation. Jin et al. [25]. compared and studied the clinical data of 30 cases of thoracoscopy combined with laparoscopic surgery and 19 cases of IVMTE. The findings indicated a significant decrease in postoperative pain score in the IVMTE group, mirroring the results reported by Wu et al. [26]. We think the primary factors are: (1) there is no chest wall incision, which reduces injury to the intercostal nerve; (2) there is no thoracic drainage tube, which reduces postoperative pain and better promotes postoperative cough and sputum excretion and early rehabilitation; and (3) during the operation, repositioning of the body and the adjustment of endotracheal intubation are avoided, and the operation time is shortened. Therefore, the compression time of the endoscope on the surrounding tissues is reduced, which also reduces the pain.

The International Pain Research Association defines postoperative chronic pain as pain caused by surgery, secondary to post-operative acute pain and lasting for more than 3 months. Currently, there is no successful remedy for persistent pain, leading to a significant decline in patients' quality of life and raising doubts about the treatment strategy.According to the literature [27], most patients with chronic pain have neuropathic pain, and a consider1able number of patients have psychogenic pain. In addition, the central and surrounding inflammatory response systems may also be involved in its pathogenesis [28]. The occurrence of postoperative acute pain without obvious pain relief may also evolve into postoperative chronic pain. The study's correlation analysis revealed a notable connection between postoperative pain at 3 and 6 months and the surgical technique, as well as the NRS score on the 14th day after the operation. There was a notable decrease in chronic pain occurrence among patients who had IVMTE and those who effectively managed pain 14 days after the operation. Inflatable mediastinoscopy also offers clear benefits in reducing pain at 3 and 6 months post-operation, specifically in decreasing the occurrence of chronic pain. We found that the main reason is that inflatable mediastinoscopy causes less tissue damage, especially without pain stimulation of the chest wall incision, and the acute pain is better controlled, thus reducing the incidence of chronic pain. In addition, patients can subjectively accept more minimally invasive surgery, and their psychological state may play a certain role in chronic pain.Reducing surgical trauma and effectively managing postoperative acute pain are crucial in decreasing the likelihood of postoperative chronic pain.

The study has the following limitations and deficiencies. This initial study is limited to a single center and a small sample size, leading to potential patient selection bias. A larger, multicenter prospective study is needed to validate these findings. Second, the postoperative chronic pain assessment of this study did not use the NRS scale to evaluate the patients. Third, the small differences in the operation between different surgeons cannot be completely avoided, which needs to be further confirmed by a multicenter prospective randomized controlled study.

5. Conclusion

IVMTE is the recommended choice for individuals with esophageal cancer receiving surgical intervention.IVMTE is more effective than MIME in decreasing both acute and chronic pain and speeding up the early recovery of patients diagnosed with early esophageal cancer.In addition, patients with postoperative pain should be intervened as soon as possible to avoid the formation of chronic pain and affect their quality of life.

Data availability statement

The dataset used and/or analyzed in this retrospective study can be obtained from the corresponding authors upon reasonable request.

CRediT authorship contribution statement

Gaoxiang Wang: Research design and writing. **Shanming Tao:** Research design and writing. **Xiaohui Sun:** Data collection and collation. **Jun Wang:** Data collection and collation. **Tian Li:** Statistical analysis and follow-up. **Zhengwei Chen:** Statistical analysis and follow-up. **Changqing Liu:** Research guidance, paper revision, and financial support. **Mingran Xie:** Research guidance, paper revision, and financial support.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Mingran Xie reports article publishing charges was provided by National Natural Science Foundation of China. Mingran Xie reports article publishing charges was provided by Anhui Provincial key research and development plan. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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