Am J Transl Res 2021;13(11):12843-12851
www.ajtr.org /ISSN:1943-8141/AJTR0137596

Original Article

Clinical efficacy of thoracoscopic surgery by subxiphoid approach for thymoma and its influence on intraoperative blood loss and postoperative complications

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Received July 22, 2021; Accepted September 27, 2021; Epub November 15, 2021; Published November 30, 2021

Abstract: Objective: To evaluate the clinical efficacy of thoracoscopic surgery by subxiphoid approach for patients with thymoma and its influence on intraoperative blood loss and postoperative complications. Methods: From January 2019 to January 2020, 90 patients who underwent thoracoscopic surgery were enrolled and evenly divided into a control group receiving surgery by lateral thoracic approach and an experimental group adopting the subxiphoid approach according to different surgical approaches, and their clinical data were retrospectively analyzed. The clinical efficacy, perioperative indexes, postoperative complications, pulmonary function, and inflammatory factors were compared between the two groups. Generic Quality of Life Inventory-74 (GQOLI-74) was used to assess the quality of life of the patients before and after surgery, and Mini-Mental State Examination (MMSE) was used to assess their mental state. The Numerical Rating Scale (NRS) was used to evaluate the postoperative pain of the two groups. Results: After treatment, the total clinical effectiveness rate of the experimental group was significantly higher than that of the control group ($P<0.05$). The experimental group obtained superior results in perioperative index and fewer postoperative complications compared with the control group ($P<0.05$). Better performance of FEV1 and FVC was observed in the experimental group than the control group ($P<0.05$). The experimental group had significantly higher postoperative GQOLI-74 scores ($P<0.001$) and MMSE scores ($P<0.05$) than the control group. Lower levels of C-reactive protein (CRP), and tumor necrosis factor-α (TNF-α), and lower NRS scores at 12 h and 24 h after surgery were witnessed in the experimental group compared to the control group ($P<0.05$). Conclusion: For patients with thymoma, the thoracoscopic surgery by subxiphoid approach is safe and effective, and can reduce the intraoperative blood loss and postoperative complications.

Keywords: Subxiphoid approach, thymoma, clinical efficacy, postoperative complications

Introduction

Thymoma is a common thoracic disease, to which the middle-aged and elderly population are most susceptible. It stems from pathological changes in thymic lymph nodes or thymic epithelial cells [1, 2], accounting for about 19-42% of mediastinal tumors. Generally, its symptoms are nonspecific in the early stage, while symptoms such as cough, swollen arms and dull pain in the chest may emerge with the advancement of the stage [3-5]. Delayed treatment may give rise to complications such as aplastic anemia and myasthenia gravis (MG), which can be life-threatening in severe cases. In light of these, early diagnosis and treatment of thymoma are of paramount significance. Surgical treatment is the main treatment for patients with confirmed thymoma, in which traditional open chest surgery is the mainstay. However, it has been criticized for major surgical trauma, massive blood loss, and pain. With the advancement of medical technology, thoracoscopic surgery by subxiphoid approach has received increasing attention owing to its features of minor trauma, minimal blood loss, shorter hospital stay, and superior clinical efficacy [6-8]. In order to investigate the clinical efficacy of thoracoscopic surgery by subxiphoid approach for patients with thymoma, and its

effects on intraoperative blood loss and postoperative complications, we performed a retrospective study on 90 patients who underwent thoracoscopic surgery from January 2019 to January 2020 in our hospital. The innovation of this research lies in the comparison of the overall curative effect of patients with different approaches of thoracoscopic surgery by comparing their lung function, quality of life, and immune factors.

General information

From January 2019 to January 2020, 90 patients who underwent thoracoscopic surgery were enrolled and evenly divided into a control group and an experimental group according to different surgical approaches, and their clinical data were retrospectively studied. Of the 90 patients, there were 44 males and 46 females, aged 61-72 years old, and 27 cases had coexistent MG. In terms of WHO pathology type, there were 27 cases of Type A, 29 cases of Type AB, and 34 cases of Type B. With regard to the clinical stage, 43 cases were in Stage I, and 47 cases were in Stage II. 46 cases had a history of drinking, and 41 cases had a history of smoking. This study was approved by the hospital ethics committee (2018-12-15).

Inclusion criteria

(1) Patients aged under 80 years old; (2) Patients with retrosternal pain, wheezing, diaphragmatic paralysis, hoarseness, and superior vena cava obstruction syndrome; There were epithelial and immature small T lymphocytes; the lobules were unclear, and the fibrous separation was not obvious; Confirmed with thymoma; (3) Patients at Masaoka clinical stage of I or II [9].

Exclusion criteria

(1) Patients with a history of pleuritis; (2) Patients with contraindications to surgery; (3) Patients with kidney or liver disease.

Methods

In the control group, thoracoscopic surgery was performed by lateral thoracic approach. Each patient was given general anesthesia on a lateral position at 30°-45° angle, with upper extremities fixed. The operation side was selected according to preoperative imaging. An incision was made between the anterior axillary line and midaxillary line at the 6th or 7th intercostal space, followed by the insertion of a 10 mm trocar through the 1 cm incision where a 30° thoracoscope was placed. Then another incision was made at the anterior axillary line at the 3rd or 4th intercostal space as an operating port with a diameter of about 3-4 cm. The protective case was placed in the operating hole, the healthy side was ventilated with one lung, and an ultrasonic knife was used to separate the adhesions. Simultaneously, the two ends of the nourishing blood vessel were clipped with a titanium clip and cut off. The thymus, tumor, and fatty tissue at the cardiophrenic angle were also completely resected [9, 10]. The incision was then sutured after the placement of a drainage tube at the observation port.

In the experimental group, thoracoscopic surgery was performed by subxiphoid approach. The procedures were as follows. With the patient at a supine position with legs apart, general anesthesia was performed, followed by placement of a single lumen endotracheal tube. Then a 2 cm subxiphoid vertical incision was made at the midline of rectus abdominis as an observational port, and 1.5 cm subcostal incisions were made at the midclavicular line bilaterally as operating ports. Carbon dioxide was injected uninterruptedly into the thoracic cavity on the operated side through a pressure of 6~8 cm H_2O, and the primary and secondary operating holes were made at the intersection of the midclavicular line and the rib arch bilaterally, with the two holes close to the rib arch. Based on the direction of the sternal angle projection, an ultrasonic knife and non-invasive forceps were used to separate the thymic tissue in the patient's mediastinal cavity and to control the scope of operation. The connective tissue behind the xiphoid was separated, an artificial pneumothorax was established in wake of the building of the sternal tunnel. An ultrasonic knife was used to cut through the mediastinal pleura, to identify and protect the phrenic nerve along the pulmonary hilum. After thymus dissection, the innominate vein was completely exposed, which was then traced and ligated while identifying the thymic artery and vein. Dissection was performed up to the superior pole of the thymus gland. After removal of thymoma and thymic tissue and dissection of mediastinal adipose tissue, the specimen was collected from the subxiphoid inci-

sion. The incision was then sutured after the placement of a drainage tube at the observation port [11].

Outcome measures

Clinical efficacy: The treatment was defined to be markedly effective if the clinical symptoms disappeared and the patient could work normally without receiving drug medication; it was defined to be effective if the dosage was reduced and an increase of weight was observed; it was defined to be ineffective if the patient's clinical symptoms were not alleviated or even worsened. Total effective rate = the rate of patients with markedly effective treatment + that of patients with effective treatment.

Perioperative indexes: Operating time, intraoperative blood loss, postoperative drainage, and hospital stay were compared between the two groups.

Postoperative complications: Pulmonary infections, wound liquefaction, and arrhythmia were compared between the two groups.

Pulmonary functions: Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) of the two groups before and after surgery were collected and analyzed.

Fasting venous blood samples in the morning were collected and centrifuged to isolate serum and then the supernatant was obtained. All serum samples were placed at -80°C, and the levels of C-reactive protein (CRP) (kit lot number: HY-E3648) and tumor necrosis factor-α (TNF-α) (kit lot number: HY-E3145) were analyzed with corresponding ELISA kits purchased from Shanghai Hengyuan Biotech Company. All procedures were conducted in strict accordance with protocols.

Generic Quality of Life Inventory-74 (GQOLI-74) Rating Scale [12] was used to evaluate the quality of life of the two groups of patients before and after surgery. It was scored from four dimensions including mental function, physical function, social function, and material life status, with the total score of 100 points. The score is positively correlated with the quality of life of the patient.

Mini-Mental State Examination (MMSE) [13] Scale was used to evaluate the mental state of patients during surgery. The total score is 30 points, and a higher score indicates a better mental state of the patient.

Numerical Rating Scale (NRS) [14] was used to assess the pain after surgery. The scale runs between 0 and 10 points, with 0 points for no pain, 1-3 for mild pain, 4-6 for moderate pain, and 7-10 for severe pain. Pain levels at 6 h, 12 h, and 24 h after surgery were labeled as T0, T1, and T2, respectively, and compared.

Statistical analyses

The data were analyzed using SPSS18.0 statistical software. The measurement data were expressed as mean ± standard deviation (SD), and t-test was used for comparison between two groups; Paired t test was used for intra-group comparison; when multiple time points were compared, the corrected *P* value was used ($P<0.05/3$); the count data were expressed as [n (%)], and χ^2 test was used for comparison between groups. The difference was considered significant if $P<0.05$.

Results

Comparison of clinical information

The clinical information demonstrated that the general information of the patients was similar between the two groups in terms of age, gender, body mass index (BMI), clinical stage, maximal tumor size, WHO pathology type, smoking or drinking history (all $P>0.05$). See **Table 1**.

Comparison of clinical efficacy between the two groups

To assess the clinical efficacy, we recorded the significantly effective, effective, and ineffective cases respectively in the two groups. Then, we observed that the total clinical effective rate after treatment in the experimental group was significantly higher than that in the control group ($P<0.05$). See **Table 2**.

Comparison of perioperative indexes

To observe the perioperative condition, we compared the perioperative indexes between the two groups using t-test. Perioperative indexes showed superior results in the experi-

Table 1. Clinical Information [n (%)]

	Experimental Group (n=45)	Control Group (n=45)	x^2 or t	P
Age (years)	65.21±1.23	65.23±1.22	0.077	0.938
Gender			0.178	0.673
Male	23 (51.11)	21 (46.67)		
Female	22 (48.89)	24 (53.33)		
BMI (kg/m^2)	25.37±1.59	25.42±1.61	0.148	0.883
Clinical Stage				
Stage I	22 (48.89)	21 (56.67)		
Stage II	23 (51.11)	24 (53.33)		
Maximal Tumor Size	4.05±1.41	4.11±1.35	0.206	0.837
WHO Pathology Type				
Type A	9 (20.00)	10 (22.22)	0.067	0.796
Type AB	10 (22.22)	11 (24.44)	0.062	0.803
Type B	13 (28.89)	11 (24.44)	0.227	0.634
Coexistent MG	14 (31.11)	13 (28.89)	0.053	0.818
Smoking			0.045	0.832
Yes	20 (44.44)	21 (46.67)		
No	25 (55.56)	24 (53.33)		
Drinking			0.178	0.673
Yes	22 (48.89)	24 (53.33)		
No	23 (51.11)	21 (46.67)		

mental group as compared to the control group (P<0.05). See **Table 3**.

Comparison of postoperative complications

To evaluate the complications, we made a comparison between the two groups regarding postoperative complications. The comparison results showed that the experimental group had lower complication rates after surgery than the control group (P<0.05). See **Table 4**.

Comparison of lung function indexes between the two groups

Table 5 shows better postoperative lung function indexes in the experimental group as compared to the control group (P<0.05).

Comparison of CRP and TNF-α level

The level of CRP was significantly lower in the experimental group in contrast to the control group (P<0.05, **Figure 1A**). The experimental group exhibited a lower level of TNF-α than the control group (P<0.05, **Figure 1B**).

Comparison of GQOLI-74 scores between the two groups

The postoperative GQOLI-74 score of the experimental group was significantly higher than that of the control group (P<0.05), indicating a more robust quality of life in the experimental group, as shown in **Figure 2**.

Comparison of MMSE scores between the two groups

The postoperative MMSE score of the experimental group was significantly higher than that of the control group (P<0.05), demonstrating an excellent mental state of the experimental group, as shown in **Figure 3**.

Comparison of NRS score

The experimental group showed a markedly lower NRS score at 12 h and 24 h after operation than the control group (P<0.05), suggesting that patients in the experimental group experienced less pain. See **Figure 4**.

Discussion

Currently, surgery is the mainstay for thymomas, and the thoroughness of resection remains the key factor influencing patients' survival [13, 14]. Traditional median sternotomy with open chest surgery is the gold standard for treatment. However, due to its disadvantages of major surgical trauma, tremendous blood loss, and high risk for complications, its application has been considerably restricted. With the advancement in medical technology, thoracoscopic surgery has captured increasing attention due to its minimally-invasive and less traumatic features and significant clinical benefits. Lateral thoracic approach was extensively used in prior surgical practice, which, however, has been criticized for its unsatisfying outcome that may give rise to intercostal nerve injury and other postoperative complications [15-17]. Prior research pointed out that compared with the transthoracic approach, the subxiphoid approach can simultaneously expose the rela-

Table 2. Comparison of clinical efficacy between the two groups [n (%)]

Groups	n	Markedly effective	Effective	Ineffective	Total effective rate
Experimental Group	45	66.67% (30/45)	31.11% (14/45)	2.22% (1/45)	97.78% (44/45)
Control Group	45	46.67% (21/45)	26.67% (12/45)	26.67% (12/45)	73.33% (33/45)
x^2					10.879
P					0.001

Table 3. Comparison of perioperative indexes ($\bar{x}$±s)

Groups	n	Operation Time (min)	Intraoperative Blood Loss (mL)	Postoperative Drainage (mL)	Hospital Stay (d)
Experimental Group	45	89.24±10.53	46.21±8.98	171.22±43.28	3.25±1.11
Control Group	45	145.25±13.75	59.47±11.12	231.82±44.37	5.29±1.38
t		21.695	6.223	6.559	7.727
P		0.001	0.002	0.001	0.002

Table 4. Comparison of postoperative complications [n (%)]

Groups	n	Pulmonary Infections	Wound Liquefaction	Arrhythmia	Total Rates
Experimental Group	45	0.00% (0/45)	2.22% (1/45)	0.00% (0/45)	2.22% (1/45)
Control Group	45	6.67% (3/45)	6.67% (3/45)	0.00% (0/45)	13.33% (6/45)
x^2					3.873
P					0.049

Table 5. Comparison of lung function indexes between the two groups (x±s)

Groups	n	FEV1 (%)		FVC (L)	
		Before surgery	After surgery	Before surgery	After surgery
Experimental Group	45	32.29±2.65	65.95±0.67	3.11±0.32	4.15±0.41
Control Group	45	32.32±157	60.55±0.32	3.12±0.29	3.52±0.31
t		0.233	3.614	0.155	8.222
P		0.817	0.001	0.877	0.001

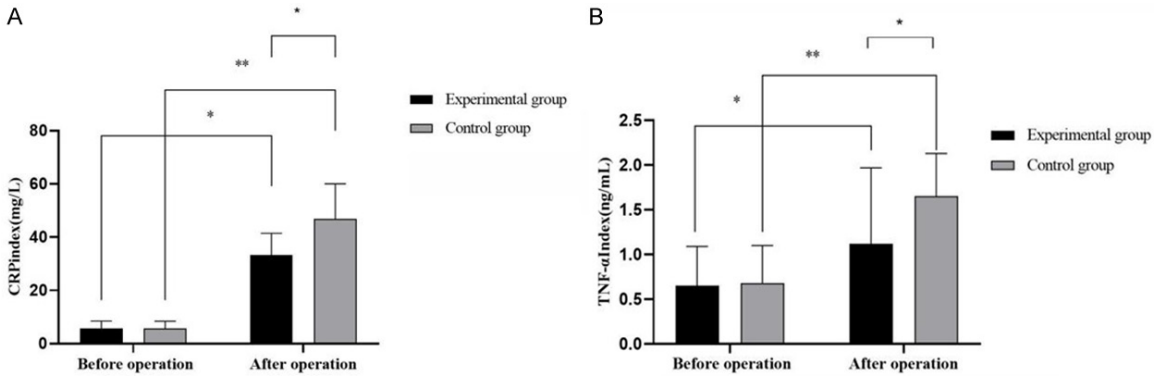

Figure 1. Comparison of CRP and TNF-α levels ($\bar{x}$±s). Note: A. The abscissa indicates Before and after operation from left to right, and the ordinate indicates the CRP level, mg/L; In the experimental group, the CRP levels before and after operation were (5.66±2.81) mg/L and (33.21±8.21) mg/L, respectively; In the control group, the CRP levels before and after operation were (5.81±2.75) mg/L and (46.78±13.25) mg/L, respectively; There was a significant difference in the CRP level before and after operation in the experimental group (t=21.298, *P<0.05); There was a significant difference in the CRP level before and after operation in the control group (t=20.309, **P<0.01); There was a significant difference in the postoperative CRP level between the two groups (t=5.840, *P=0.001). B. The

abscissa indicates before and after operation from left to right, and the ordinate indicates the TNF-α level, ng/mL; In the experimental group, the TNF-α levels before and after operation were (0.65±0.44) ng/mL and (1.12±0.85) ng/mL, respectively; In the control group, the TNF-α levels before and after operation were (0.68±0.42) ng/mL and (1.65±0.48) ng/mL, respectively; There was a significant difference in the TNF-α level before and after operation in the experimental group (t=3.294, *P=0.001); There was a significant difference in the TNF-α level before and after operation in the control group (t=10.202, **P<0.01); There was a significant difference in the postoperative TNF-α level between the two groups (t=3.642, *P=0.001).

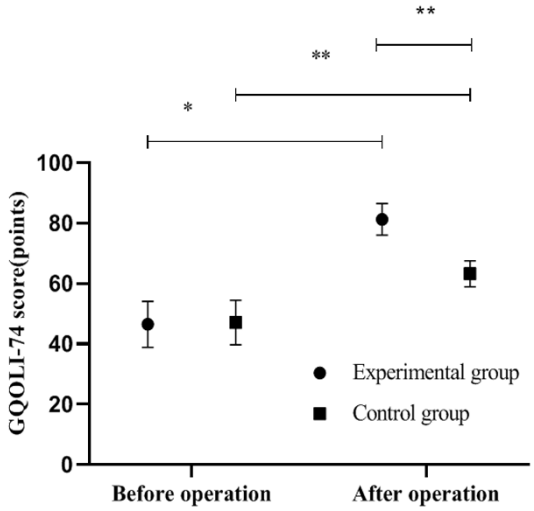

Figure 2. Comparison of GQOLI-74 scores between the two groups ($\bar{x}$±s). Note: The abscissa represents before and after operation from left to right, and the ordinate represents GQOLI-74 score, points; The GQOLI-74 scores of the experimental group before and after surgery were (46.52±7.62) points and (81.27±5.23) points, respectively; The GQOLI-74 scores of the control group before and after surgery were (47.11±7.38) points and (63.25±4.26) points, respectively; The GQOLI-74 scores of the experimental group before and after surgery were significantly different (t=25.223, *P<0.05); There was a significant difference in the GQOLI-74 scores of patients in the control group before and after surgery (t=12.706, **P<0.01); There was a significant difference in the GQOLI-74 scores between the two groups of patients after surgery (t=17.921, **P<0.01).

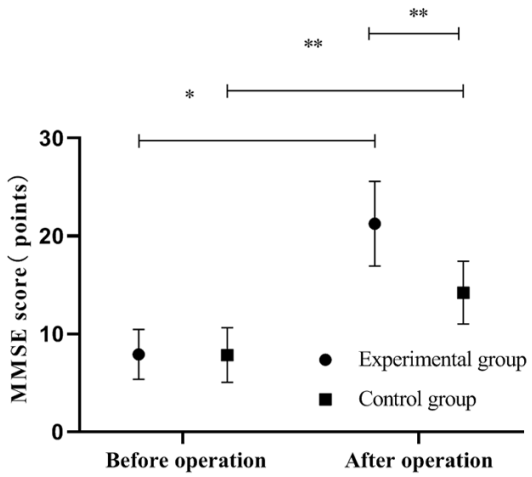

Figure 3. Comparison of MMSE scores between the two groups ($\bar{x}$±s). Note: The abscissa represents before and after operation from left to right, and the ordinate represents MMSE score, points; The MMSE scores of the experimental group before and after surgery were (7.92±2.55) points and (21.26±4.32) points, respectively; The MMSE scores of the control group before and after surgery were (7.85±2.78) points and (14.22±3.21) points, respectively; There was a significant difference in the MMSE score of patients in the experimental group before and after surgery (t=17.839, *P<0.05); There was a significant difference in the MMSE scores of patients in the control group before and after surgery (t=10.063, **P<0.01); There was a significant difference in the MMSE scores of the two groups of patients after surgery (t=8.775, **P<0.01).

tionship between the surrounding large veins and the anterior mediastinum, reduce the intractable pain to the intercostal nerves, and ensure safer dissection of bilateral adipose tissue and complete tumor removal [18, 19]. In our study, the experimental group outperformed the control group in terms of both perioperative indexes and postoperative complications (both P<0.05), suggesting that thoracoscopic surgery by subxiphoid approach could decrease the risk of blood loss and postoperative complications. In terms of the subxiphoid approach, the separation of the patient's thymus from the posterior sternal space serves to increase the thymus activity. For dissociating the upper pole of the thymus, the lower part of the thymus can be dissociated first, and then distracted downward. Moreover, the tissue around the upper pole was incised with an ultrasonic knife, and the upper pole of the thymus was completely stripped by blunt pushing and peeling. Reasonable use of an ultrasonic scalpel for sharp separation and hemostasis during the operation can reduce the amount of intraoperative blood loss and achieve "blood-free surgical field". The disadvantages of subxiphoid approach are as follows. First, there

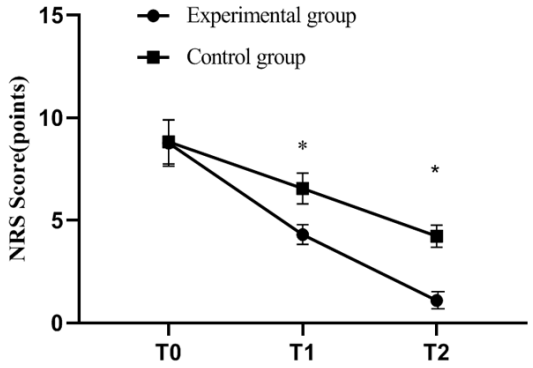

Figure 4. Comparison of NRS score ($\bar{x}$±s). Note: The abscissa indicates time intervals T0, T1, and T2 from left to right, and the ordinate indicates NRS score, points; In the experimental group, NRS scores at T0, T1, and T2 were (8.77±1.12), (4.31±0.48) and (1.09±0.18) points, respectively; In the control group, NRS scores at T0, T1, and T2 were (8.83±1.08), (6.56±0.75) and (4.23±0.54) points, respectively; There was a significant difference in NRS score at T1 between the two groups (t=16.950, *P=0.017); There was a significant difference in NRS score at T2 between the two groups (t=37.005, *P=0.017).

could be interference during instrumentation procedures and dissection of fat tissue around the cardiophrenic angle. Second, the operation is challenged by limited operating field [20, 21]. Last but not least, surgeons should be alert that 1-3 branches would return back to left innominate vein when dealing with thymic veins, for which ultrasonic ligation should be performed. In this study, patients who received surgery by the subxiphoid approach were in a supine position, which requires no position change. In addition, single lumen endotracheal intubation, two-lung ventilation, and small incision all contributed to promising outcomes including less abdominal or intercostal nerve injury, diminished complication rates, and robust recovery [23, 24]. The transthoracic approach or thoracoscopic surgery by the xiphoid process for patients with thymoma will cause damage to the patient's body functions. Detection of patients' inflammatory factor levels can objectively reflect the effectiveness of different surgical approaches. The preoperative levels of CRP and TNF-α were similar between the two groups, but after surgery, the comparison revealed more desirable results in the experimental group. The results further indicated that there was less surgical trauma and inflammatory response in surgery by subxiphoid approach, which contributes to a favorable recovery in patients with thymoma. In addition, the FEV1 and FVC also showed more satisfying results in the experimental group compared to the control group, which was in agreement with the results from Yano et al. [25] who revealed that postoperative FEV1 and FVC were (2.85±0.42)% and (4.13±0.35) L respectively in the observation group, significantly higher than those of the control group. Taken together, the thoracoscopic surgery by subxiphoid approach contributes to better pulmonary outcome, less pain, and rapid recovery. The limitation of this study was that there was no long-term follow-up trial with a large sample size, and the data obtained are biased. In the future, the sample size will be expanded, randomized controlled trials will be conducted, and multi-factor analysis will be performed to determine the factors that affect the prognosis.

In conclusion, the thoracoscopic surgery by subxiphoid approach can reduce intraoperative blood loss, shorten hospital stay, and diminish postoperative complication rates.

Disclosure of conflict of interest

None.

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