



Short-term analysis of uniport video-assisted thoracoscopic surgery via the subxiphoid approach without chest tube drainage for anterior mediastinal tumors: a comparative retrospective study

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Background: Uniport video-assisted thoracoscopic surgery (VATS) via the subxiphoid approach has emerged as a safe and effective treatment for anterior mediastinal tumors. However, there is limited evidence of the necessity of chest tubes and the comparative efficacy with other approaches.

Methods: A total of 141 patients with anterior mediastinal tumors receiving VATS were enrolled in this retrospective study. The patients were divided into the lateral approach (LA) group, the uniport subxiphoid approach (USA) group, and the three-port subxiphoid approach (TSA) group. Short-term analysis including operation time, chest tube rates, drainage duration, visual analogue scale (VAS) score, and hospital stay were compared. Postoperative CT scans were analyzed to evaluate the amount of pleural effusion.

Results: There was no significant difference in demographic and baseline characteristics among the three groups (all $P > 0.05$). The operation time, blood loss, and hospital stay of the subxiphoid approach group were significantly lower than the LA group ($P < 0.001$). The postoperative CT scans demonstrated that the USA group had a similar amount of pleural effusion as the other groups ($P = 0.1605$). The postoperative VAS score of the USA group was significantly lower than the other groups ($P < 0.001$). There was no significant difference in complications, in-hospital death, and conversion to thoracotomy among the three groups (all $P > 0.05$).

Conclusions: VATS via the subxiphoid approach is less invasive, equally safe, and same effective for anterior mediastinal tumors than the LA. The chest tube could be omitted for the USA.

Keywords: Subxiphoid approach; video-assisted thoracoscopic surgery (VATS); uniport; three-port; anterior mediastinal tumors; short-term efficacy

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Introduction

Anterior mediastinal tumor is a common disease in thoracic surgery, and surgical resection has been widely applied as the primary treatment strategy (1). Traditional median sternal incision can well expose the anterior mediastinum tissue, which has long been the “gold standard” operation

to treat anterior mediastinal diseases. However, this surgical method causes massive trauma to the patient, leading to prolonged postoperative recovery and a significant impact on respiratory and circulatory function (2). In recent years, traditional median sternal incision has been gradually replaced by video-assisted thoracoscopic surgery (VATS).

Compared with traditional sternotomy, the VATS not only shortens the hospital stay and thoracic drainage time with less invasiveness but also achieves the same treatment efficacy with non-inferior overall survival and recurrence rate (3,4). Despite the relatively limited exposure, VATS through the lateral approach (LA), has achieved satisfying efficacy for the treatment of anterior mediastinal tumors. Especially for patients with Masaoka stage I–II thymoma, the 5-year overall survival has achieved comparable results with thoracotomy (5). However, VATS through the LA still has certain limitations.

Through the LA (intercostal), the thoracoscope the contralateral phrenic nerve and the upper pole of the thymus, increasing the risk of intraoperative damage to phrenic nerve-related blood vessels. On the other hand, the intercostal nerve injury caused by the intercostal incision is inevitable, resulting in chronic postoperative intercostal neuralgia and skin paresthesia in the nerve distribution area (6). Suda *et al.* proposed a surgical approach via the subxiphoid approach, which effectively avoided intercostal nerve injury (7). Establishing artificial pneumothorax through CO₂ increases the anterior mediastinal space and provides a safer surgical operation environment. Simultaneously, the visual field of thoracoscopy placed in the center direction can reveal the bilateral phrenic nerve and the upper pole of the thymus, hence obtaining visual field exposure similar to open thoracotomy. According to the number of ports, the subxiphoid approach can be divided into three-port and uniport. Nevertheless, there is limited evidence of the efficacy and safety of subxiphoid approach VATS for anterior mediastinal tumors, especially a comparison of three-port and uniport incisions. In this study, we retrospectively analyzed 141 cases with anterior mediastinal tumors who received VATS resection and aimed to explore the advantages and disadvantages of different surgical approaches. We present the following article in accordance with the STROBE reporting checklist (available at <https://dx.doi.org/10.21037/atm-21-5790>).

Methods

Study cohort and clinical data

We retrospectively reviewed all patients undergoing VATS resection for anterior mediastinal tumors from Jan 2016 to Jan 2021 and screened patients meeting the following inclusion criteria: (I) patients were adults (≥ 18 years old); (II) patients were diagnosed with an anterior mediastinal tumor

and undergoing VATS resection; (III) patients had complete clinical data and CT scan files. The exclusion criteria were as follows: (I) patients who received median sternotomy; (II) patients who had malignant tumors with apparent invasion to neighboring organs.

Ethical statement

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Renji Hospital, Shanghai Jiaotong University School of Medicine (No. 2017-082). Individual consent for this retrospective analysis was waived.

Surgical technique

LA

As previously described, we used the classic three-port intercostal approach (7). The patients were placed in a supine position. Three skin incisions were made on the anterior axillary line in the third intercostal space, the anterior axillary line, and the midaxillary line in the fifth intercostal space. In most cases, the anterior mediastinal tumor was approached from the right side of the chest. When the tumor was predominantly on the left side, the tumor was approached from the left side of the chest. For patients with myasthenia gravis (MG) or positive anti-acetylcholine receptor antibodies, we adopted the lateral intercostal approach from both sides to remove all adipose tissue anterior to both phrenic nerves (*Figure 1A*).

Three-port subxiphoid approach (TSA)

The patient was placed in the lithotomy position. After disinfection, a 3–4 cm transverse or vertical incision was made under the xiphoid. The sternum was bluntly separated from the anterior mediastinum, and a thoracoscope was inserted. A 0.5–1 cm surgical incision was made at the junction of the bilateral midclavicular line and the costal arch, and a trocar was placed close to the costal arch toward the xiphoid. Artificial pneumothorax was made with CO₂ pressure of 8–10 mmHg. The bilateral pleura was opened with an ultrasonic knife to enter the bilateral thoracic cavity. The loose connective tissue of the anterior mediastinum along the sternum's posterior edge was thoroughly dissected until the left innominate vein's level. The bilateral phrenic nerves were fully exposed, and the mediastinal pleura along the phrenic nerve was ultimately opened. On the right side,

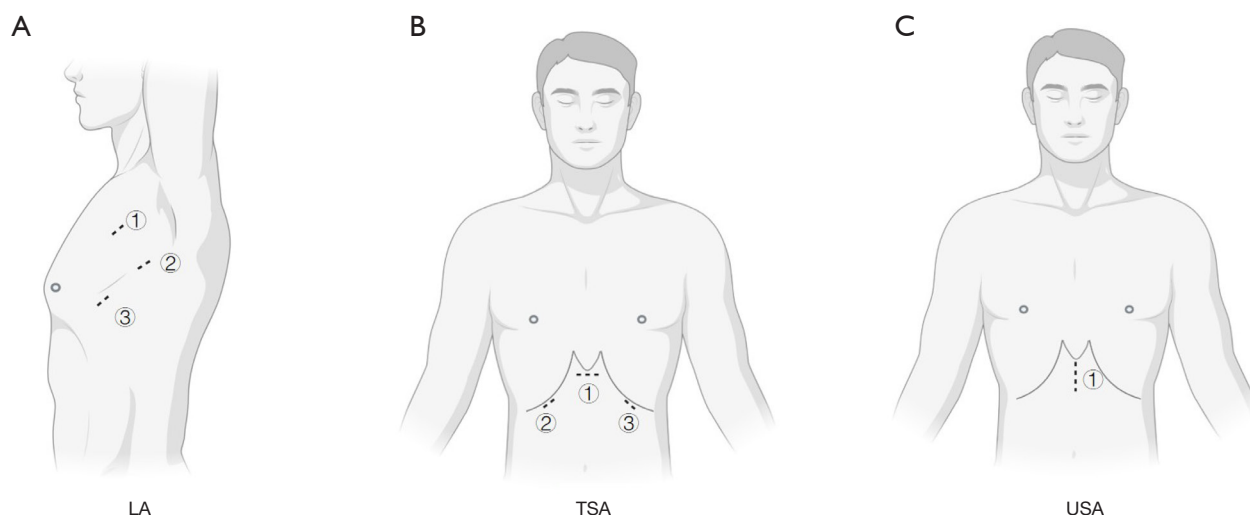


Figure 1 The skin incisions of the three approaches. (A) The LA: ① 1 cm incision at the anterior axillary line in the third intercostal space as the operating port; ② 1 cm incision at the midaxillary line in the fifth intercostal space as the observational port; ③ 0.5 cm incision at the anterior axillary line in the fifth intercostal space as the operating port; (B) the TSA: ① 3 to 4 cm transverse or vertical incision under the xiphoid process as the observational port; ②③ a 0.5–1 cm incision at the intersection of the bilateral midclavicular line and the costal arch as the operating hole; (C) the USA: ① 3 to 4 cm transverse or vertical incision under the xiphoid process. LA, lateral approach; TSA, three-port subxiphoid approach; USA, uniport subxiphoid approach.

the left innominate vein was exposed along the superior vena cava. The left innominate vein and bilateral upper poles of the thymus were carefully dissociated from right to left. The thymic veins were cut off with an ultrasonic knife. The specimen was taken out from the major incision under the xiphoid (*Figure 1B*).

Uniport subxiphoid approach (USA)

Only 1 transverse or vertical skin incision of 3–4 cm was made beneath the xiphoid, and the subsequent procedures were the same as the TSA (*Figure 1C*).

Chest tube placement

After the surgery, the chest tube was placed in the incision and connected to the negative pressure drainage ball. The lung was re-expanded by the anesthesiologist until no air leaked before the incision was closed. For patients with minor wounds and bleeding, the chest tube was removed immediately after the drain site was sutured.

Postoperative management

All patients were extubated after the surgery and transferred to the ward. Bedside chest radiography was

routinely conducted to monitor postoperative bleeding, pneumothorax, and pleural effusion on the day of surgery. Blood examination was performed on the first and third postoperative days (PODs). Postoperative analgesia, including intravenous tramadol, oral nonsteroidal analgesics, and acetaminophen, was administered. The visual analogue scale (VAS) was applied to evaluate postoperative pain on the first 3 PODs. For patients with MG, the same medications used preoperatively were continued after the operation under the guidance of the neurologist. A CT scan was also conducted 2–3 days after the surgery. The chest tube would be removed if the drainage was less than 200 mL/day and the lung was wholly recruited.

Data collection

All data were collected from the hospital's electronic record system. Demographic characteristics and clinical data were collected, including age, gender, body mass index (BMI), tumor type, tumor size, MG, and comorbidities. Short-term outcomes of all patients, including operation time, blood loss, conversion to thoracotomy, in-hospital death, hospital stays, chest tube drainage, postoperative VAS score, and complications, were also investigated. Two independent radiologists were invited to download and analyze the

postoperative CT scan DICOM files of all patients to assess the amount of pleural effusion.

Statistical analysis

SPSS ver. 21.0 (IBM SPSS Statistics, Chicago, IL, USA) was used to perform all statistical analyses. Continuous variables are presented as mean \pm standard deviation (SD). Categorical variables are presented as numbers (percentages). Analysis of variance (ANOVA) was conducted to compare continuous variables meeting the normal distribution among the three groups, while the least significant difference (LSD) *t*-test was used for the post-hoc test. The Chi-square test was performed to compare categorical variables of different groups, while partitions of the Chi-square test were adopted as the method for the post-hoc test. A *P* value less than 0.05 was considered statistically significant.

Results

Demographic and baseline characteristics

A total of 141 patients were enrolled in this study, including 51 patients who received VATS through the LA (LA group), 57 patients who received VATS through the USA (USA group), and 33 patients who received VATS through the TSA (TSA group). As shown in *Table 1*, we compared the demographic and baseline characteristics of the three groups. There was no significant difference among the three groups in demographic data, including age, gender, BMI, and comorbidities (all $P > 0.05$). We also found that the three groups demonstrated similar tumor type proportions ($P = 0.640$). Most patients (64.5%) were diagnosed with thymoma in the three groups. There was also no difference in WHO type and Masaoka stage among the three groups ($P > 0.05$). Fourteen patients (9.9%) were complicated by MG.

Short-term outcomes

The short-term outcomes of the three groups were compared, as shown in *Table 2*. No in-hospital death occurred. Only 1 patient in the USA group was converted to open thoracotomy due to major bleeding, while there was no difference in the incidence of conversion to thoracotomy among three groups ($P = 0.476$). The subxiphoid approach demonstrated a significant advantage in less blood loss, operation time, and hospital stay, whether in the USA or

TSA group (all $P < 0.001$). However, there was no statistical difference in blood loss, operation time, and hospital stay between the USA and TSA groups (both $P > 0.05$). As for postoperative pain, we found that the USA group presented a lower VAS score than the other two groups at POD1 and POD2, but not POD3. The TSA and LA groups showed no significant differences in postoperative complications, including phrenic nerve paralysis, effusion/pneumothorax requiring thoracocentesis, and dyspnea (all $P > 0.05$). In terms of laboratory results, white blood cell count (WBC), C-reactive protein (CRP), and hemoglobin (Hgb) showed no significant differences among the three groups at POD1 and POD3 (all $P > 0.05$).

Chest tube and drainage

We also compared the chest tube rates of the three groups and the drainage, as shown in *Table 2*. During the operation, the surgeon would decide whether to place the chest tube or not according to their experience. We summarized the chest tube rates of the three groups and found that the USA group had the lowest chest tube rate of 21.1% ($P < 0.001$). The postoperative drainage from the chest tube was comparable among the three groups, as well as the drainage duration (both $P > 0.05$). We used CT to calculate the amount of pleural effusion in the three groups and found no significant difference (*Figure 2*) ($P = 0.1605$).

Discussion

Recent years have witnessed the surging development of minimally invasive approaches in thoracic surgery. Despite the gold standard of median sternotomy in thymectomy for anterior mediastinal tumors, VATS has emerged as the most frequently used procedure due to its minimal invasiveness (8,9). This study retrospectively compared three VATS approaches for anterior mediastinal tumors, including their short-term outcomes, surgery-related indicators, and postoperative pleural effusion amount. Three significant findings were made in this study: (I) the subxiphoid approach had a shorter operation time, less blood loss, and shorter hospital stay than the LA; (II) patients who received uniport incisions had lower VAS scores than patients with three-port incisions; (III) uniport patients without chest tubes did not have a higher amount of pleural effusion and thoracocentesis.

Anterior mediastinal tumors are the most common mediastinal tumors (10). Surgical resection has always

Table 1 Demographic and clinical characteristics of the three groups

Variables	LA (n=51)	Subxiphoid approach		F/ χ^2	P
		USA (n=57)	TSA (n=33)		
Demographics					
Age (y)	52.5±11.7	56.8±18.5	57.4±13.0	1.451	0.238
Gender (male), n (%)	19 (37.3)	13 (22.8)	11 (33.3)	2.814	0.245
BMI (kg/m ²)	22.3±2.4	23.2±2.5	22.2±2.9	2.656	0.074
Tumor type, n (%)				6.067	0.640
Thymoma	33 (64.7)	37 (64.9)	21 (63.6)		
Thymic cyst	16 (31.4)	14 (24.6)	8 (24.2)		
Teratoma	0 (0.0)	2 (3.5)	1 (3.0)		
Squamous cell carcinoma	0 (0.0)	3 (5.3)	1 (3.0)		
Other	2 (3.9)	1 (1.8)	2 (6.1)		
Thymoma WHO type*, n (%)				10.106	0.120
A	5 (15.2)	8 (21.6)	6 (28.6)		
AB	11 (33.3)	7 (18.9)	3 (14.3)		
B1–3	13 (39.4)	22 (59.5)	9 (42.9)		
C	4 (12.1)	0 (0.0)	3 (14.3)		
Thymoma Masaoka stage*, n (%)				3.530	0.473
I	11 (33.3)	8 (21.6)	9 (42.9)		
Ila	16 (48.5)	23 (62.2)	10 (47.6)		
IIb	6 (18.2)	6 (16.2)	2 (9.5)		
Tumor size (diameter, cm)	3.64±2.45	3.60±2.26	4.28±2.28	1.024	0.362
MG, n (%)	3 (5.9)	7 (12.3)	4 (12.1)	1.464	0.481
Comorbidities, n (%)					
Hypertension	11 (21.6)	12 (21.1)	9 (27.3)	0.519	0.772
Diabetes	10 (19.6)	13 (22.8)	5 (15.2)	0.773	0.679
COPD	4 (7.8)	3 (5.3)	2 (6.1)	0.307	0.858
Coronary heart disease	2 (3.9)	4 (7.0)	2 (6.1)	0.494	0.781

Continuous variables are presented as mean ± SD. Categorical variables are presented as n (proportions). *, percentage of cases with thymoma. LA, lateral approach; USA, uniport subxiphoid approach; TSA, three-port subxiphoid approach; BMI, body mass index; MG, myasthenia gravis; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

been the preferred treatment option (11). The surgical route of the median sternum incision is still the primary surgical method for treating anterior mediastinal tumors. This surgical method can clearly show the structure of the anterior mediastinum, which helps clarify the relationship between the tumor and the mediastinal vessels. The surgery is still the first choice for tumors involving

the mediastinum's essential structures (12), though this surgical approach is very traumatic and significantly impacts the patient's cardiopulmonary function. As more and more benign and early malignant mediastinal diseases are discovered and diagnosed, the shortcomings of median sternotomy have gradually increased. At the same time, minimally invasive VATS technology is

Table 2 Perioperative data and in-hospital outcomes

Variables	LA (n=51)	Subxiphoid approach		F/ χ^2	P
		USA (n=57)	TSA (n=33)		
Operation time (min)	123.1±38.0	90.1±17.8*	100.4±23.0*	18.584	<0.001
Conversion to thoracotomy, n (%)	0 (0.0)	1 (1.8)	0 (0.0)	1.484	0.476
Blood loss (mL)	53.7±15.5	44.4±9.4*	43.8±10.7*	9.879	<0.001
In-hospital death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	N/A	N/A
Hospital stay (d)	4.6±1.4	3.5±0.5*	3.9±0.8*	17.474	<0.001
Chest tube, n (%)	51 (100.0)	12 (21.1)*	30 (90.9) [#]	86.661	<0.001
Chest tube drainage (mL)					
POD1	221.4±46.0	211.7±34.9	227.0±55.6	1.370	0.256
POD2	181.7±47.4	164.2±49.7	176.0±59.4	1.624	0.200
Duration of drainage (d)	2.0±0.8	1.6±0.5	1.9±0.8	1.346	0.266
Postoperative VAS score					
POD1	4.9±1.5	3.7±1.5*	5.3±1.3 [#]	15.958	<0.001
POD2	3.8±1.7	2.6±1.7*	4.3±1.5 [#]	13.639	<0.001
POD3	2.7±1.7	2.0±1.3	2.6±1.9	2.563	0.081
Complications, n (%)					
Phrenic nerve paralysis	1 (2.0)	0 (0.0)	0 (0.0)	1.777	0.411
Effusion/pneumothorax requiring thoracocentesis	0 (0.0)	2 (3.5)	1 (3.0)	1.760	0.415
Dyspnea	1 (2.0)	2 (3.5)	3 (9.1)	2.631	0.268
WBC ($\times 10^9/L$)					
POD1	12.0±2.6	11.3±2.3	11.9±2.5	1.149	0.320
POD3	9.8±2.9	9.5±2.0	9.9±2.6	0.305	0.738
CRP (U/L)					
POD1	56.7±19.2	47.0±16.4*	58.2±19.8 [#]	5.349	0.006
POD3	12.1±8.0	12.3±4.4	12.6±8.9	0.068	0.934
Hgb (g/L)					
POD1	126.7±12.1	131.0±6.7	129.6±11.1	2.580	0.079
POD3	121.5±12.8	126.5±7.3	124.3±11.5	3.020	0.052

Continuous variables are presented as mean \pm SD. Categorical variables are presented as n (proportions). Subxiphoid approach vs. LA, *, $P < 0.05$; three-port vs. uniport, [#], $P < 0.05$. LA, lateral approach; USA, uniport subxiphoid approach; TSA, three-port subxiphoid approach; VAS, visual analogue scale; POD, postoperative day; WBC, white blood cell count; CRP, C-reactive protein; Hgb, hemoglobin; SD, standard deviation.

developing fast. VATS via the LA has been widely used in the treatment of anterior mediastinal tumors. Compared with median sternotomy, VATS via the LA has minor trauma characteristics and results in quick recovery after

the operation (9), but this surgical method still has its shortcomings. For the unilateral approach, whether it is a single or three-port approach, it is difficult to expose the contralateral phrenic nerve, the upper pole of the thymus,

and the fatty tissue at the heart-phrenic angle, which increases intraoperative injury and residual risk. Especially for cases with MG, the residual thymus and surrounding adipose tissue are not conducive to alleviating myasthenia symptoms and even induces myasthenic crisis (13). Some studies have proposed that the bilateral thoracoscopic approach for treating anterior mediastinal tumors with MG can completely remove the thymus and surrounding adipose tissue and effectively relieve the symptoms of myasthenia (14-16). However, bilateral thoracoscopic surgery requires changing the patient's position during the operation, which significantly prolongs the operation time and increases the occurrence of postoperative complications. At the same time, due to possible intercostal nerve damage caused by the LA, the incidence of intercostal nerve paralysis and neuralgia increased significantly (17).

Suda *et al.* proposed a new VATS approach to remove the thymus through the subxiphoid approach, effectively avoiding intercostal nerve injury and reducing postoperative intercostal nerve pain (7). We successfully applied this surgical approach to treat anterior mediastinal tumors without surrounding tissue invasion or limited local invasion. There were no cases of perioperative death. Only 1 patient was converted to open-chest surgery due to massive bleeding caused by incidental injury of the left innominate vein. According to the number of ports, the subxiphoid approach could be divided into uniport and three-port types. For the uniport approach, a 3 to 5 cm transverse or vertical incision is made just over the xiphoid process's prominence depending on the width of the angle between the subcostal margins (14) (*Figure 1C*). For the three-port approach, a thoracoscope for observation of the operation area is inserted through an incision of about 3-4 cm under the xiphoid, with two 0.5-1cm incisions at the intersection of the bilateral midclavicular line and the costal arch as the operating hole to insert the trocar (*Figure 1B*). Artificial pneumothorax pressure of 8-10 mmHg expands the anterior mediastinum space to better display the surgical field of vision.

Through 90 cases of VATS via the subxiphoid approach within 5 years, we found that this procedure can expose the bilateral phrenic nerves, avoiding phrenic nerve injury caused by inadequate visual field exposure during the operation. Simultaneously, the surgical approach is satisfactory for the exposure of the bilateral thymus and the upper pole of the thymus. The complete removal of the bilateral thymus and surrounding adipose tissue is significant for anterior mediastinal disease with myasthenia

symptoms. Eleven surgical cases with muscle weakness symptoms in this study were effectively relieved after the operation. We also found that the subxiphoid approach groups had significantly lower operation times, blood loss, and hospital stays than the LA group (all $P < 0.001$), indicating that the subxiphoid approach was less invasive and more helpful for postoperative recovery. Mao *et al.* also compared the subxiphoid and intercostal approaches in anterior mediastinal tumor surgery. They found that the VAS score was lower in patients who underwent the subxiphoid approach than in the intercostal group. Postoperative drainage time, postoperative drainage volume, and hospitalization time were significantly increased in the left thoracic approach group compared with the right thoracic approach group (6). According to previous reports, the most likely complication of the LA approach is phrenic nerve paralysis, while for the subxiphoid approach, it is dyspnea (18). The incidence of postoperative complications is very low and does not affect long-term pain. This study also found a very low incidence of postoperative complications, with no statistical difference among the three groups.

Furthermore, we found that the USA group had a lower VAS score than the TSA group. The primary reason is that most patients in the USA group (45/57) did not have chest tube placement after the surgery. The chest tube is one of the significant reasons for postoperative pain (19). We found that the USA approach led to better exposure and hemostasis during our subxiphoid approach, making the omission of chest tubes possible. To ensure safety, we conducted routine bedside X-rays, laboratory tests, and CT scans. No severe postoperative bleeding or pneumothorax was found in all patients. We also used CT scan reconstructions to estimate the amount of pleural effusion, which indicated no statistical difference among the three groups. Li *et al.* also found no difference between patients with or without chest tubes regarding the incidence of dyspnea and delayed pleural effusion requiring thoracentesis after chest tube removal (20). Recent studies have witnessed the progress of VATS surgical technique via subxiphoid approach, including the non-intubation, "four-zone one-way" method, which further decreased the trauma and enhanced the postoperative recovery (21,22).

Several limitations of this study must be noted. First, this study was a retrospective study, and selection bias could not be avoided even with no statistical difference in baseline characteristics. We've tried to apply the propensity score match to mitigate the baseline bias, but this method was only

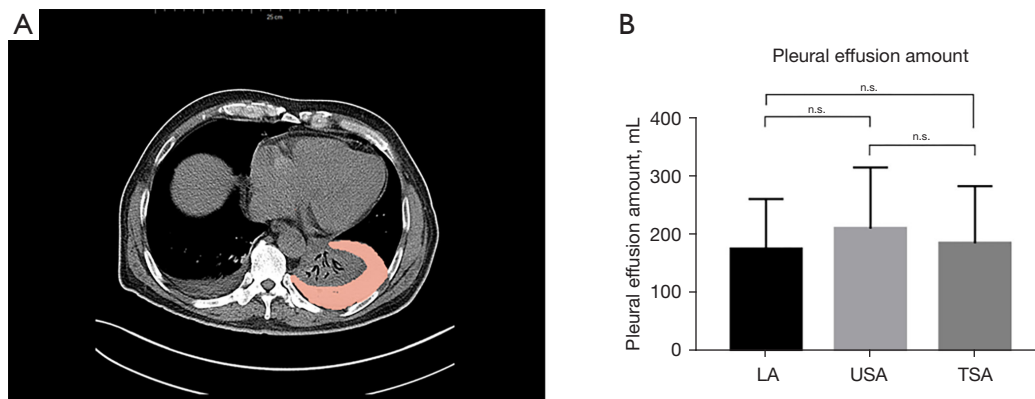


Figure 2 The postoperative CT scan results and estimated pleural effusion amounts. (A) Pleural effusion depicted by CT scan software; (B) pleural effusion amount estimation of the three groups. LA, lateral approach; USA, uniport subxiphoid approach; TSA, three-port subxiphoid approach; n.s., not significant.

suitable for two groups. What's more, the demographical data and baseline characteristics were comparable among the three groups, indicating the bias was under control, which might not influence the final results (23). Also, the sample size of this study was relatively small, and all patients were from a single center, which lowered the evidence level. A prospective, multicenter clinical trial with more patients might be required to validate the conclusions. Second, the long-term outcome of the surgery was not included because of the lack of follow-up results. Whether the approach affects the long-term survival of patients with anterior mediastinal tumors needs further investigation. Lastly, the learning curve and the surgeon's experience could impact the results, which should be taken into consideration.

Conclusions

The subxiphoid approach is less invasive and equally effective in VATS surgery for anterior mediastinal tumors. For the subxiphoid approach, the uniport approach leads to less pain and reliable hemostasis when the omission of the chest tube is feasible.

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Footnote

Reporting Checklist: The authors have completed

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Data Sharing Statement: Available at <https://dx.doi.org/10.21037/atm-21-5790>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Renji Hospital, Shanghai Jiaotong University School of Medicine (No. 2017-082). Individual consent for this retrospective analysis was waived.

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