



# Preliminary evaluation and discussion of the safety of left innominate vein resection

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**Background:** To evaluate the safety of resection of anterior mediastinal lesions involving the left innominate vein (LIV) and analyze the risk factors affecting LIV resection safety.

**Methods:** Patients who underwent anterior mediastinal lesion and LIV resection from January 2010 to December 2018 in the Department of Thoracic Surgery of Tangdu Hospital, Air Force Medical University, were followed up, and preoperative, intraoperative and postoperative factors were analyzed.

**Results:** Forty-eight patients who underwent anterior mediastinal lesion and LIV resection from January 2010 to December 2018, except for 2 who died of lung infection-induced respiratory failure, were followed up, with an average follow-up time of 32 months (range, 6–72 months). Postoperative: in 31 cases (67.39%), patients did not manifest LIV resection-associated complications; in 15 cases (32.61%), patients manifested mild LIV resection-associated complications; no patient manifested severe LIV resection-associated complications. The average operation time, average blood loss and average hospitalization time were 155.17 min, 324.13 mL and 11.83 days, respectively. Univariate analysis showed that the degree of LIV invasion and surgical approach were risk factors for predicting LIV resection safety.

**Conclusions:** For anterior mediastinal lesions involving the LIV, LIV resection is a simple, safe and effective surgical procedure.

**Keywords:** Anterior mediastinal lesion; resection of left innominate vein (resection of LIV); safety

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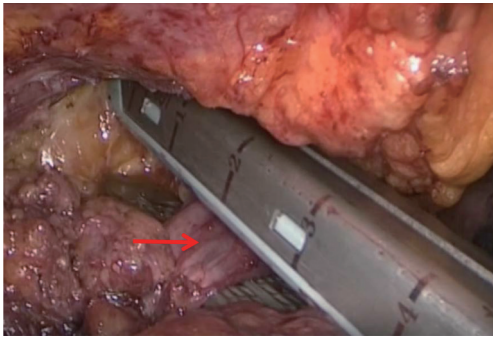
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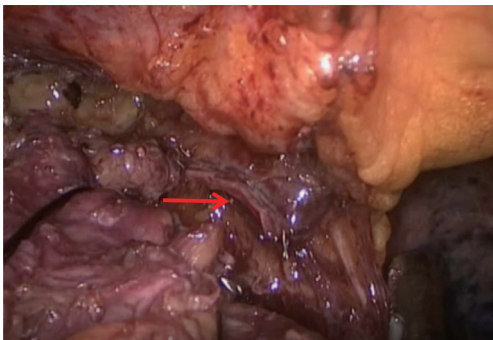
## Introduction

The anterior mediastinum is a narrow area between the anterior edge of the trachea and pericardium and the sternum, including the thymus and large blood vessels that enter and exit the heart. Anterior mediastinal lesions are uncommon but can occur at any age but are more common to those 30–40 years of age; of anterior mediastinal lesions,

thymomas are the most common, followed by mediastinum-type lung cancer, lymphoma, and neuroblastic tumors (1,2). They often involve the large blood vessels of the thoracic cavity, especially the superior vena cava and its branches, and the left brachiocephalic (innominate) vein (LIV), because it crosses the anterior mediastinum, is susceptible to invasion (3–6). For some patients, surgery may be the only feasible approach of achieving long-term survival (7–14). The safety



**Figure 1** Resection of the invaded distal LIV with a vascular closure device (the arrow shows the LIV). LIV, left innominate vein.



**Figure 2** Residual of the LIV (distal end, arrow). LIV, left innominate vein.

and effectiveness of LIV resection in patients with LIV invasion have not been assessed adequately (6,15,16). In this study, we retrospectively analyzed the clinical data of 48 patients with anterior mediastinal lesions involving the LIV who underwent anterior mediastinal lesion and LIV resection, evaluated the safety of LIV resection alone and analyzed the possible influencing factors. The results are reported below.

## Methods

### General information

Data from patients who underwent anterior mediastinal lesion and LIV resection in the Department of Thoracic Surgery of Tangdu Hospital, Air Force Medical University, from January 2010 to December 2018 were retrospectively analyzed. Preoperatively, all patients underwent enhanced chest computed tomography (CT) to determine LIV

involvement and stenosis severity. They also underwent complete blood count analysis, blood gas analysis, cardiac ultrasonography, electrocardiography (ECG), and analysis of liver and kidney function, electrolytes, coagulation series, and pulmonary function to exclude surgical contraindications. Our Ethical Committee was informed of the study and did not require approval. All patients gave their informed consent for the study.

### Postoperative safety evaluation criteria of LIV resection

LIV resection may lead to venous return blockage and blood stasis in the drainage area, causing swelling of the left upper limb and face, engorgement of the left jugular vein, varicosity in the left anterior chest wall and upper abdomen, left periorbital edema, conjunctival hyperemia, blurred vision of the left eye, and cerebral edema-derived dizziness, headache, convulsions, and disturbance of consciousness (15,16). “Safety” is defined as no LIV resection-associated complications and no manifestation of the above-described symptoms; “Danger” is defined as the manifestation of severe LIV resection-associated complications (tissue necrosis in the left upper limb, sensory and motor dysfunction, convulsions, impaired vision, and disturbance of consciousness); and “Relative safety” is defined as the manifestation of mild LIV resection-associated complications (the above-described symptoms but no serious complications).

### Categorization of LIV stenosis severity

With reference to William Sandford’s classification of superior vena cava stenosis, we categorized the severity of LIV stenosis as follows: (I) grade I (mild to moderate): partially obstructed LIV (degree of stenosis <90%); (II) class II (severe): almost completely obstructed LIV (degree of stenosis ≥90%); and (III) grade III (complete stenosis): completely obstructed LIV, i.e., preoperative imaging data show no blood flow in the LIV.

### Surgical method and postoperative treatment

Anterior mediastinal lesions were resected laparoscopically using the “three-hole” operation via the subxiphoid and subcostal arch approach, and the invaded LIV was removed intraoperatively through the proximal and distal end by closure resections with a vascular closure device (Figures 1,2). Thoracotomy (including conversion of laparoscopic

surgery to open surgery) was used to remove the invaded anterior mediastinal lesion via a vertical incision in the sternum, and the invaded LIV was closed or incised via ligation intraoperatively using a vascular closure device and a suture, respectively, at the proximal and distal ends. All patients were returned to the intensive care unit (ICU) with tracheal intubation and ventilator assistance and injected subcutaneously with low-molecular-weight heparin sodium (0.4 mL/day) within 24 hours after surgery.

### *Postoperative follow-up and treatment*

Patients were followed up regularly after surgery and subjected to various comprehensive treatments (e.g., radiotherapy and chemotherapy) according to their respective pathological types.

### *Statistical analysis*

Univariate analysis was performed using the statistical software package SPSS 20.0, in which count data were analyzed using the  $\chi^2$  and Fisher tests, and the measurement data were analyzed using the *t*-test.

## **Results (see Tables 1-3)**

### *General information*

Among the 48 patients, 2 died perioperatively of septic shock derived from pulmonary infection and thus were excluded from the follow-up. The remaining 46 patients were followed up for an average of 32 months (range, 6–72 months); 20 were male, and 26 were female, with an average age of 50.35 years (range, 27–72 years), a preoperative mean body mass index (BMI) of 24.02 kg/m<sup>2</sup> (range, 17–35 kg/m<sup>2</sup>), a preoperative mean platelet count of 195.29×10<sup>9</sup>/L [range, (101–412)×10<sup>9</sup>/L], and a preoperative mean hemoglobin level of 127.75 g/L (range, 109–156 g/L). Nineteen patients manifested hypertension, diabetes, myasthenia gravis, and anemia. Twenty-two patients underwent “three-hole” laparoscopic surgery via the subxiphoid and subcostal arch approach, and 24 patients underwent open surgery via a vertical incision in the sternum, with an average operation time of 155.17 min (range, 90–260 min), an average blood loss of 324.13 mL (range, 10–1,000 mL) and an average length of hospital stay of 11.83 days (range, 6–19 days). Postoperative pathological examination indicated the following diagnoses: 5 cases

of squamous mediastinum, 4 cases of adenocarcinomas mediastinum, 2 cases of seminoma, 2 cases of type A thymoma, 7 cases of type AB thymoma, 8 cases of type B1 thymoma, 8 cases of type B2 thymoma, 4 cases of type B3 thymoma, 3 cases of breast cancer, and 3 cases of other diseases. Eleven patients manifested various postoperative complications such as pulmonary infection, pleural effusion, atelectasis, and myasthenic crisis and were all discharged after the complications were treated.

### *Safety of LIV resection*

Postoperatively, 31 patients (67.39%) did not show any LIV resection-related complications, 15 patients (32.61%) showed mild LIV resection-related complications, and no patients (0.00%) showed severe LIV resection-related complications.

### *Factors affecting the safety of LIV resection*

Based on the safety of LIV resection, the patients were divided into 2 groups: a “Safety” group and a “Relative Safety” group. Analyses of the 2 groups indicated statistically significant differences in LIV invasion and its severity (*P*=0.01), surgical procedure (*P*<0.01), left half-perimeter and right half-perimeter of the anterior chest wall at days 1, 3 and 5 after surgery (*P*<0.01), and left median cubital venous pressure at days 1, 3 and 5 after surgery (*P*<0.01) but showed no differences in sex, age, BMI, preoperative platelet count, preoperative hemoglobin, preoperative comorbidities, intraoperative blood loss, operative time, average hospital stay, postoperative pathology, and postoperative complications (Table 1). Multivariate logistic regression analysis suggested that the degree of LIV invasion and surgical approach were risk factors for predicting LIV resection safety.

### *Comparison of perioperative outcomes of “three-hole” laparoscopic surgery via the subxiphoid and subcostal arch approach and open surgery via a vertical incision in the sternum*

The comparison of perioperative outcomes of “three-hole” laparoscopic surgery via the subxiphoid and subcostal arch approach and that of the open surgery via a vertical incision in the sternum indicated no differences in sex, age, BMI, degree of preoperative LIV invasion, preoperative platelet count, preoperative hemoglobin level, preoperative

**Table 1** Univariate analysis of clinical data and safety of LIV resection

Clinical information	Total/average	Safety (n=31)	Relative safety (n=15)	P
Sex				0.76
Female	26	18	8	
Male	20	13	7	
Age (year)	50.35±16.17	49.84±16.61	50.37±10.36	0.56
BMI (kg/m <sup>2</sup> )	24.02±5.95	24.07±3.47	23.86±4.93	0.74
LIV invasion and severity				0.01
I	29	15	14	
II	10	9	1	
III	7	7	0	
Preoperative platelet count (×10 <sup>9</sup> /L)	195.29±14.12	201.71±15.28	194.62±7.67	0.83
Preoperative hemoglobin (g/L)	127.75±27.96	126.82±24.41	129.87±19.32	0.74
Preoperative comorbidities				0.90
Yes	19	13	6	
No	27	18	9	
Surgical approach				<0.01
Laparoscopic surgery via the subxiphoid and subcostal arch approach	22	19	3	
Open surgery via a vertical incision in the sternum	24	12	12	
Operation time (min)	155.17±49.17	140.50±27.28	165.00±44.81	0.18
Intraoperative blood loss (mL)	324.13±309.20	306.66±294.27	334.28±297.68	0.19
Average hospital stay	11.83±3.94	9.42±2.75	12.75±2.59	0.12
Postoperative pathological diagnosis				1.00
Squamous cell carcinoma	5	3	2	
Adenocarcinoma	4	3	1	
Seminoma	2	1	1	
Type A thymoma	2	1	1	
Type AB thymoma	7	5	2	
Type B1 thymoma	8	5	3	
Type B2 thymoma	8	6	2	
Type B3 thymoma	4	3	1	
Thymic carcinoma	3	2	1	
Other	3	2	1	
Other postoperative complications				1.00
Yes	11	7	4	
No	35	24	11	

**Table 1** (continued)

Table 1 (continued)

Clinical information	Total/average	Safety (n=31)	Relative safety (n=15)	P
Difference of the median circumference between the left and the right forearm (mm)				
1 day before surgery	0.11±0.10	0.05±0.13	0.03±0.01	0.36
1 day after surgery	2.12±1.78	0.17±0.14	8.85±4.78	<0.01
3 days after surgery	4.18±2.12	0.18±0.14	12.98±6.55	<0.01
5 days after surgery	4.01±1.65	0.17±0.17	10.54±6.38	<0.01
30 days after surgery	0.10±0.07	0.07±0.11	0.18±0.13	0.82
Left median cubital venous pressure (cmH <sub>2</sub> O)				
1 day before surgery	10.34±4.63	12.04±3.78	8.84±2.46	0.24
1 day after surgery	16.56±5.98	14.83±4.45	20.36±8.19	<0.01
3 days after surgery	22.84±5.24	18.64±9.93	27.33±8.56	<0.01
5 days after surgery	21.04±7.11	18.01±8.76	25.65±6.83	<0.01
30 days after surgery	13.54±5.24	13.31±4.48	13.75±4.27	0.64
Follow-up time/months	32.34±13.10	32.21±13.35	33.25±13.74	0.65

comorbidities, and postoperative pathology but showed significant differences in intraoperative blood loss ( $P<0.01$ ), operation time ( $P<0.01$ ), average hospital stay ( $P<0.01$ ), and other postoperative complications ( $P<0.01$ ) (Table 2).

## Discussion

Anterior mediastinal tumors often involve the superior vena cava and the left and right innominate veins and cause superior vena cava syndrome in severe cases (3-5,17). Artificial vascular replacement or pericardial patch repair are difficult and risky, and in the 1970s, superior vena cava syndrome was often listed as a surgical contraindication, for which conservative treatment was recommended (18). After nearly 4 decades, with the improvement in diagnostic and surgical techniques and the extensive application of vascular substitutes, breakthroughs have been made regarding operations on patients with superior vena cava syndrome, and the removal of the superior vena cava and (or) the left and right innominate veins and vessel replacement or bypass through artificial blood vessels have made it possible for radical resection of tumors or have relieved superior vena cava obstruction (11,12,17,19-23). For cases in which the anterior mediastinal lesion simply invades the LIV and phleboplasty cannot be performed, what are the options? Artificial vascular replacement or LIV resection? The former conforms to the physiology and is conducive

to blood return but is associated with unfavorable factors such as surgical trauma, long operation time, high surgical difficulty, and the need for long-term anticoagulation; the latter is simple, fast, and minimally invasive, but its safety and postoperative blood return pathway have not been thoroughly investigated (6,15,16) but were explored in this study.

We found that postoperatively, 67.39% of patients with LIV resection did not show any LIV resection-related complications and that 32.61% of the patients showed mild LIV resection-related complications, mostly left upper limb swelling, mild headache, and dizziness; no patient (0.00%) showed severe LIV resection-related complications, e.g., tissue necrosis in the left upper limb, sensory and motor dysfunction disorders, convulsions, impaired vision and disturbance of consciousness, etc. The symptoms were more severe on days 3, 4 and 5 after surgery and then gradually diminished, lasting approximately 1 month, which was consistent with the changes in the Difference of the median circumference between the left and the right forearm and the left median cubital venous pressure at days 1, 3, 5 and 30 after surgery.

The LIV is formed by the confluence of the left internal jugular vein and left subclavian vein posterior of the left sternoclavicular joint, accommodating venous blood flow in the left internal jugular vein, left subclavian vein, left vertebral vein, left internal thoracic vein, and inferior

**Table 2** Comparison of the perioperative outcomes of the “three-hole” laparoscopic surgery via the subxiphoid and subcostal arch approach and those of open surgery via a vertical incision in the sternum

Clinical information	Total/average	Laparoscopic surgery (n=22)	Open surgery (n=24)	P
Sex, n				0.80
Female	26	12	14	
Male	20	10	10	
Age (year)	50.35±16.17	50.23±20.03	50.44±17.92	0.64
BMI (kg/m <sup>2</sup> )	24.02±5.95	25.11±9.78	23.03±10.86	0.55
LIV invasion and severity				0.19
I	29	17	12	
II	10	3	7	
III	7	2	5	
Preoperative platelet count (×10 <sup>9</sup> /L)	195.29±14.12	189.22±23.51	201.33±21.75	0.77
Preoperative hemoglobin (g/L)	127.75±27.96	124.33±19.83	130.12±28.05	0.89
Preoperative comorbidities				0.58
Yes	19	10	9	
No	27	12	15	
Operation time (min)	155.17±49.17	110.32±31.56	212.32±41.35	<0.01
Intraoperative blood loss (mL)	324.13±309.20	52.76±23.27 (range, 10–100)	525.47±203.77 (range, 200–1,000)	<0.01
Average hospital stay	11.83±3.94	7.82±3.86 (range, 6–10)	12.95±5.29 (range, 7–19)	0.02
Postoperative pathological diagnosis, n				0.99
Squamous cell carcinoma	5	3	2	
Adenocarcinoma	4	1	3	
Seminoma	2	1	1	
Type A thymoma	2	1	1	
Type AB thymoma	7	3	3	
Type B1 thymoma	8	4	4	
Type B2 thymoma	8	3	5	
Type B3 thymoma	4	2	2	
Thymic carcinoma	3	1	2	
Other	3	2	1	
Other postoperative complications, n				0.02
Yes	11	2	9	
No	35	20	15	
Follow-up time/months	32.34±13.10	34.45±12.63	30.01±10.94	0.65

thyroid vein and collecting venous blood flow from the left head and neck, left upper limb and left chest (except the heart) and part of the left upper abdominal wall (15). After

LIV resection, the related blood return pathways may be as follows: (I) communicating branches of the left and right innominate vein: the left and right innominate veins have



**Table 3** Analysis of the relationship between the degree of LIV stenosis and the difference of the median circumference between the left and the right forearm and that between the degree of LIV stenosis and the left median cubital venous pressure

Clinical information	I (n=29)	II (n=10)	III (n=7)
Difference of the median circumference between the left and the right forearm (mm)			
1 day before surgery	0.03±0.01	0.04±0.03	0.05±0.07
1 day after surgery	5.74±6.54*	0.11±0.06 <sup>#</sup>	0.05±0.04 <sup>#</sup>
3 days after surgery	8.64±7.86*	0.14±0.85 <sup>#</sup>	0.10±0.05 <sup>#</sup>
5 days after surgery	7.34±6.77*	0.13±0.80 <sup>#</sup>	0.10±0.02 <sup>#</sup>
30 days after surgery	0.13±0.12	0.04±0.09	0.06±0.02
Left median cubital venous pressure (cmH <sub>2</sub> O)			
1 day before surgery	8.67±3.63	9.54±4.86	14.07±3.76
1 day after surgery	23.24±5.97*	14.55±9.74 <sup>#</sup>	14.26±4.24 <sup>#</sup>
3 days after surgery	29.48±7.53*	15.87±6.23 <sup>#</sup>	13.87±3.57 <sup>#</sup>
5 days after surgery	28.72±8.93*	15.65±8.45 <sup>#</sup>	14.22±3.43 <sup>#</sup>
30 days after surgery	13.55±4.08	13.45±4.64	13.94±3.86

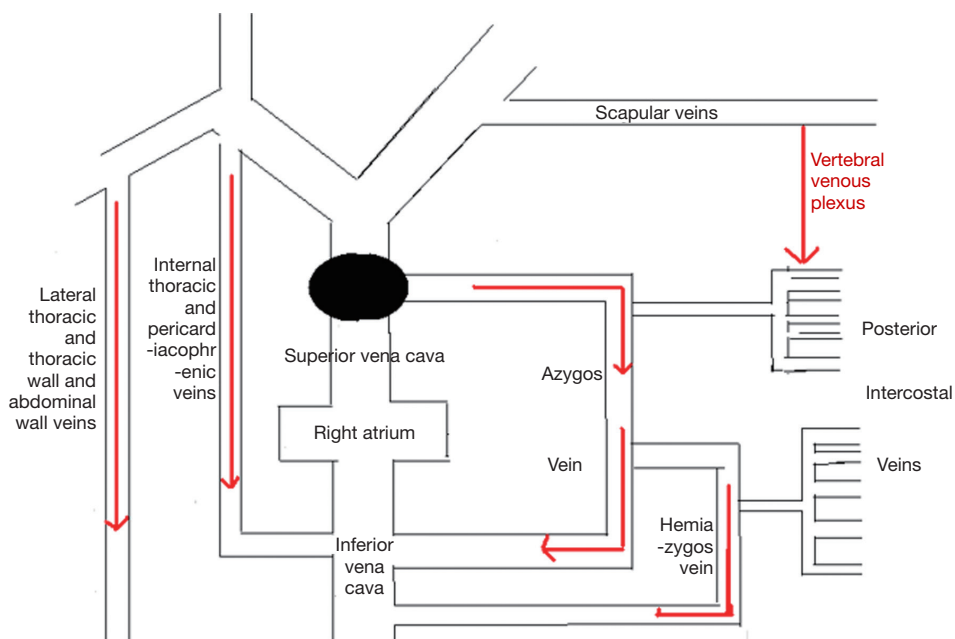
<sup>#</sup>, P<0.05 vs. I (n=29); \*, P<0.05 vs. 1 day before surgery.

extensive communicating branches in the cranium, the face, the neck, and between the deep and superficial veins of the upper chest wall, and when the LIV is chronically obstructed, the venous blood collected by the LIV from the left head and neck, the left chest, and part of the left upper abdominal wall can be returned to the right innominate vein (24); (II) communicating branches of the superior and inferior vena cava (*Figure 3*): there are several important communicating branches between the superior and inferior vena cava (16,25-27), including the azygos venous system, the internal thoracic and pericardiophrenic veins, and the lateral thoracic and thoracic wall and abdominal wall veins (28,29), of which the azygos venous system consists of the azygos vein, accessory azygos vein, and accessory hemiazygos vein and mainly collects blood flow from the shoulder and back veins, the vertebral venous plexus and the posterior intercostal veins and connects the LIV and the superior and inferior vena cava. The communicating branches of the superior vena cava and the azygos venous system are important pathways for acute LIV obstruction and venous return in the left upper limb (*Figures 3-5*).

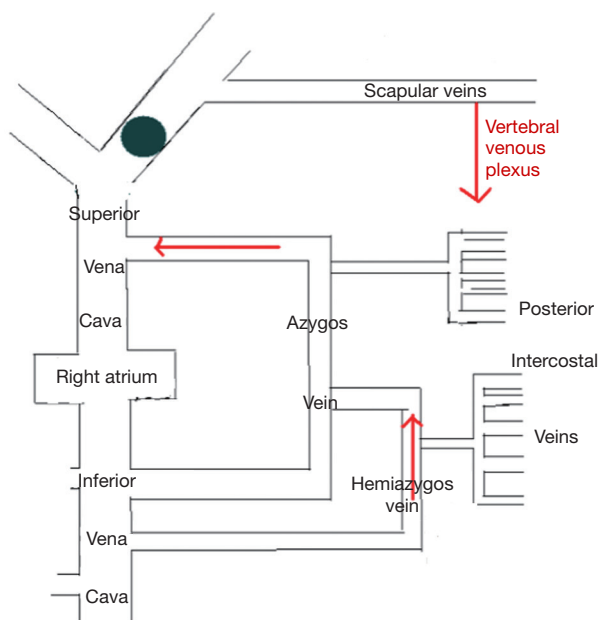
In this study, we found that the preoperative degree of LIV stenosis is an important factor for the safety of LIV resection. Based on the results in *Table 3*, with grades II and III LIV stenosis, the Difference of the median circumference between the left and the right forearm and the left median cubital venous pressure on days 1, 3, or

5 were not significantly different from those the day before surgery, suggesting that in the case of severe or complete obstruction of LIV, blood return and venous communicating branches have already formed preoperatively; therefore, LIV removal has no effect on blood circulation. In the case of grade I LIV stenosis, the Difference of the median circumference between the left and the right forearm and the left median cubital venous pressure on days 1, 3, or 5 were significantly greater than those the day before surgery. Furthermore, for grades II and III LIV stenosis, the results suggest that with moderate LIV stenosis, the removal of the LIV may cause LIV resection-related complications in the formation process of collateral circulation after surgery.

With the rapid development of thoracoscopic techniques, video-assisted thoracoscopic surgery (VATS) has been widely used in the resection of anterior mediastinal lesions. Compared with traditional open surgery, thoracoscopic surgery has the advantages of less trauma, less bleeding, quicker recovery, fewer complications, etc. and is thus a safer and more effective procedure. In this study, we also found that compared with open surgery via a vertical incision in the sternum, laparoscopic surgery had a shorter operation time, less intraoperative blood loss, and shorter average hospital stay, with fewer LIV resection-associated complications (*Table 2*). In particular, “three-hole” laparoscopic surgery via the subxiphoid and subcostal arch approach (30-34) can reduce damage to the communicating



**Figure 3** Communicating branches of the superior and inferior vena cava.



**Figure 4** Azygos venous system.

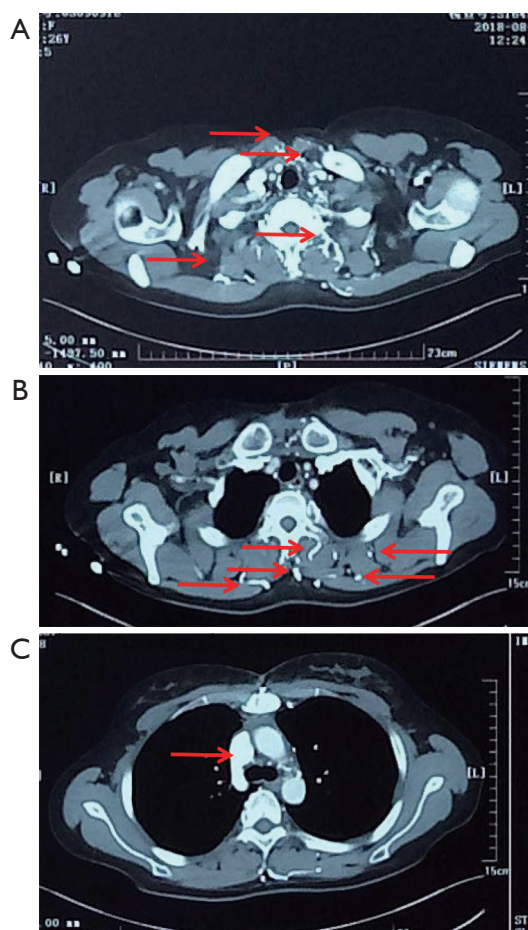
branches of the chest wall and is conducive to the protection of the left internal thoracic vein and the pericardiacophrenic vein under direct vision during surgery, which reduces the incidence of postoperative blockage of blood return. Certainly, the choice of surgical approach is more

dependent on the location and size of lesions in the anterior mediastinum, and under the premise of full assessment of the preoperative conditions and when conditions permit, laparoscopic surgery via the subxiphoid and subcostal arch approach should be clinically promoted.

**Conclusions**

Our extensive literature survey indicated that for superior vena cava obstruction, artificial vascular replacement has been mostly adopted while simple LIV resection has been mentioned rarely, without examination of its safety (6,15,16). In this study, we retrospectively analyzed the clinical cases of anterior mediastinal lesion and LIV resection in our hospital and concluded that LIV resection is a relatively simple, safe and effective surgical procedure. Although some patients may develop mild complications such as left upper limb swelling and dizziness, the complications can be effectively treated with diuretics, reduction in intracranial pressure and anticoagulation therapy. The degree of LIV invasion and laparoscopic surgery are safe factors for LIV resection-associated complications. Because this study is a retrospective analysis, there are limitations such as bias, and the findings should be verified through multicenter, large-scale prospective randomized controlled trials.





**Figure 5** Images from a 27-year-old woman taken at the time of reexamination 1 month after anterior mediastinal lesion and LIV resection. Her postoperative pathological diagnosis was type B2 thymoma. (A) Communicating branches of the deep and superficial veins of the neck; (B) communicating branches of veins of the shoulder and back; (C) thickened azygos vein.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*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. Our Ethical Committee was informed of the study and did not require approval. All patients gave their informed consent for the study.

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