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ORIGINAL ARTICLE

Analysis of giant thoracic neoplasms: Correlations between imaging, pathology and surgical management

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Computed tomography angiography; giant thoracic neoplasm; surgical management; three-dimensional reconstruction.

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Abstract

Background: A giant thoracic neoplasm is extremely rare and poorly understood. Our systemic study introduced computed tomography angiography (CTA) with three-dimensional (3D) reconstruction imaging and evaluated correlations between imaging, pathology, and surgical management.

Methods: Data from 45 patients undergoing surgery for giant thoracic neoplasm in our institution between May 2007 and November 2015 were collected. The clinical characteristics, imaging manifestations, preoperative biopsy, surgical management, postoperative pathology, and prognosis and their correlation were analyzed.

Results: The clinical characteristics, imaging manifestations, and pathological types were complicated. Four patients underwent CTA with 3D reconstruction imaging and feeding vessels were found in three cases. Twenty-four selected patients accepted preoperative biopsy, eight of which were inconsistent with postoperative pathology. Complete resection was performed in 39 cases, 20 of which underwent extended excision. The median survival duration of all patients was 58 months (range 3.0–118.0). The one, three, and five-year survival rates were 86.0%, 64.4%, and 47.0%, respectively. Univariate analyses showed tumor size and resection status were prognostic factors for survival ($P = 0.003$ and $P < 0.001$, respectively).

Conclusions: A giant thoracic neoplasm should preferably be treated in experienced centers for precise diagnosis and optimal therapy schemes with comprehensive consideration of clinical characters, imaging manifestations, pathology, surgical management, and prognosis. Innovative CTA with 3D reconstruction imaging together with preoperative biopsy are feasible and effective in therapeutic decision-making and surgical planning. Complete surgical resection remains the mainstay of curative therapy for all resectable tumors.

Introduction

A giant thoracic neoplasm is extremely rare. In our clinical practice, a number of patients with giant thoracic neoplasms were hospitalized, which raised our concern. At present, there is no unified standard for the clinical diagnosis of giant thoracic neoplasm because of its rarity, heterogeneity, and pleomorphism. Generally, large tumors of >10 cm in diameter or occupying more than 40% of the hemithorax are regarded as giant thoracic neoplasms.[1,2] The clinical characteristics, imaging manifestations, surgical management, pathology, and prognosis are poorly understood and to the best of our knowledge, little systemic research has been conducted.

The key points of therapy are to determine whether surgery is necessary and to ensure perioperative safety. A conventional enhanced computed tomography (CT) scan is the gold standard for imaging assessment. CT angiography (CTA) with three-dimensional (3D) reconstruction imaging and even rapid prototyping is expected to facilitate anatomic study, simulation, and planning for thoracic

surgery.[3,4] High-quality 3D-CT imaging, which clearly reveals the anatomy of pulmonary vessels and bronchi, could play an important role in safe, efficient, minimally invasive pulmonary anatomical resection.[5] Thus, we introduced CTA with 3D reconstruction imaging and biopsy pathology to selected patients for better assessment and surgery planning.[6]

The primary aim of our study was to retrospectively analyze the clinical characteristics, imaging manifestations, surgical management, pathology, and prognosis of giant thoracic neoplasms. The secondary aim was to evaluate the effectiveness and feasibility of CTA with 3D reconstruction imaging and biopsy pathology in the preoperative assessment.

Methods

Eligibility criteria and data collection

Medical records of adult patients undergoing surgical resection for giant thoracic neoplasm in our institution between May 2007 and November 2015 were retrospectively reviewed. All patients were evaluated by a multidisciplinary team and treated with curative intent. The inclusion criteria were as follows: (i) thoracic neoplasms >10 cm in greatest diameter, (ii) surgical resection was performed for curative intent, (iii) no neoadjuvant chemoradiotherapy had been administered, and (iv) the patient was followed-up for more than a year. The exclusion criteria were as follows: (i) thoracic neoplasms <10 cm in greatest diameter, and (ii) non-surgical treatment. Patient data was collected by two independent investigators, with a third investigator auditing data capture to minimize missing data and control concordance, as well as the inclusion or exclusion of patients. Missing or inconsistent data were obtained from original medical records or by telephone call with the corresponding surgeon or patient. The regional institutional review board approved this study, and written informed consent was obtained from all patients or their guardians, as appropriate.

Computed tomography angiography (CTA) with three-dimensional (3D) reconstruction imaging

Patients underwent iodine allergy tests and then a spiral CT scan with a Toshiba 320-slice volume CT scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan). A total of 75 mL of iohexol (Omnipaque, 300 mg of iodine per mL; GE Healthcare, Shanghai, China) was injected through the upper extremity via intravenous bolus injection with a mechanical injector (REF XD 2051; Ulrich GmbH & Co KG, Buchbrunnenweg, Germany) at a rate of 2.5–3.0 mL/s without subsequent injection of saline solution. The slice thickness was 0.5 mm. Digital imaging data were transferred to the Vitrea workstation using post-processing procedures such as volume rendering, maximum intensity projection, and multiplanar reconstruction. The innovative imaging technique was recommended to selected patients with solid lesions abundant in blood supply or suspected unresectable tumors.

Preoperative biopsy

Preoperative pathologic diagnosis was recommended to selected patients through image-guided transthoracic needle core biopsy (CT or ultrasonic) or bronchoscopy. The least invasive biopsy with the highest yield is preferred.

Follow-up

All patients were followed up with clinical visits (preferred) or telephone contact. During follow-up clinical examination, a chest CT was taken every 6–12 months for the first two years, followed by annual chest CT. In cases of suspected recurrence, chest enhanced CT and biopsy were performed to obtain unequivocal radiologic and pathological proof. One patient died from cerebral hemorrhage on the 15th postoperative day, leaving 44 patients with survival data for analyses. Overall survival was calculated from the date of surgery to the date of death or last follow-up (15 November 2016).

Statistical analysis

Statistical analysis was performed using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). Overall survival was calculated using the Kaplan–Meier method, and statistical significance was evaluated using a log-rank test. Statistical significance was considered when $P < 0.05$.

Results

Patient demographic data

Demographic data are presented in Table 1. Twenty-five men and 20 women were included in the study. The median age at diagnosis was 41 years. The majority of patients had been suffering symptoms such as chest tightness, shortness of breath, dyspnea, cough, and chest pain before consultation. Four patients had shown superior vena cava syndrome prior to diagnosis.

Four patients underwent CTA with 3D reconstruction imaging and feeding vessels were found in three of the cases. The details of positive findings and intraoperative verification are elaborated in Figures 1–3. Further details of

Table 1 Demographic data

Variables	Values
Age (years)	45 (16–79)
Gender	
Male	25 (55.56%)
Female	20 (44.44%)
Smoking history	
Smoker	12 (26.67%)
Non-smoker	33 (73.33%)
Main complaint	
Asymptomatic†	11 (24.44%)
Chest tightness, shortness of breath, dyspnea	14 (31.11%)
Cough, pectoralgia	16 (35.56%)
SVCS	4 (8.89%)
Course duration	
Within 1 month	10 (22.22%)
1–3 months	12 (26.67%)
3–6 months	8 (17.78%)
6 months to 1 year	4 (8.89%)
More than 1 year	11 (24.44%)
CT imaging	
Conventional contrast-enhanced CT	41
CTA with 3D reconstruction	4
Preoperative biopsy	
Transthoracic needle core biopsy	23
Electronic bronchoscopy	1
Negative	21

†Identified by either health examination screening or incidental discovery without any symptoms. 3D, three-dimensional; CTA, computed tomography angiography; SVCS, superior vena cava syndrome.

feeding vessels, local tumor expansion, and loco-regional invasion on high-resolution 3D imaging were helpful to surgeons in assessing the feasibility of complete surgical resection.

Twenty-four patients (53.33%) accepted preoperative biopsy through image-guided transthoracic needle core biopsy (n = 23) or electronic bronchoscopy (n = 1). However, two cases were still unclear, even after biopsy was attempted twice. Eight cases were inconsistent with postoperative pathology, including three cases of germ cell tumors, one of fibrosarcoma, one of pulmonary sarcomatoid carcinoma, one of leiomyoma of esophagus, one of solitary fibrous tumor and one case of non-Hodgkin lymphoma.

Surgical data

The surgical data are presented in Table 2. The surgery performed included median sternotomy in 11 patients, left posterolateral thoracotomy in 14, right posterolateral thoracotomy in 11, left anterolateral thoracotomy in four, right anterolateral thoracotomy in three and T-shaped incision in two patients. Complete resection was performed in 39 cases, 20 of which underwent extended excision. Exploratory

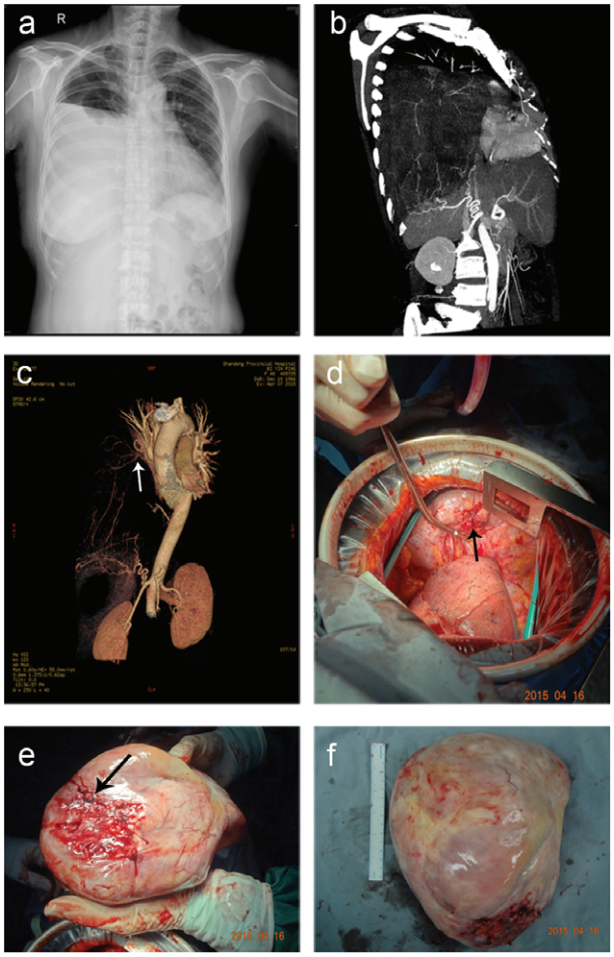

Figure 1 (**a**) A giant thoracic neoplasm was located in the right hemithorax. (**b**) Large numbers of tortuous vessels were found within the tumor body and on the surface of the adjacent diaphragm on a contrast-enhanced computed tomography scan. Vessels in the upper portion of the tumor seemed to be closely related to branches of the right upper pulmonary artery. (**c**) An aberrant artery originating from the right renal artery was distributed into the right side of the diaphragm and thoracic tumor body. (**d,e**) As confirmed by surgery, the tumor was solitary and completely encapsulated with a wide-basement vascular pedicle from the diaphragm. Ligation and suture of the pedicle was followed by complete resection. (**f**) The resected specimen measured 23 × 20 × 11 cm^3 and weighed about 3.0 kg. Pathology revealed solitary fibrous tumor of the pleura.

thoracotomy was performed in two cases. Preoperative biopsy pathology was highly suspected to be solitary fibrous tumor and lipoma, respectively. After exploratory thoracotomy, frozen pathology revealed malignant soft tissue sarcoma and thus was impossible to completely resect. Palliative resection was performed in four cases because of the involvement of great vessels (thoracic aorta, aortic arch, or pulmonary trunk). The postoperative pathology results were liposarcoma, fibrosarcoma, synovial sarcoma, and thymic squamous cell carcinoma, respectively.

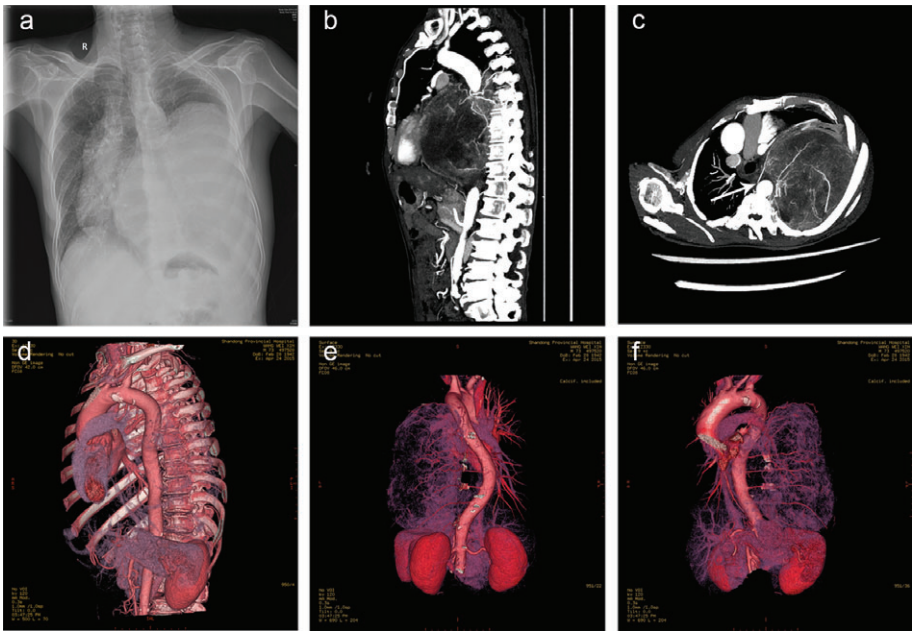

Figure 2 (**a**) A giant thoracic neoplasm was located in the left hemithorax. (**b,c**) Large numbers of tortuous vessels were found within the tumor body in the arterial phase, especially in the posterior of the tumor body. An aberrant artery originating from the anterior wall of the thoracic aorta travelled forward and downward along the right side of the tumor body (see white arrow). (**d–f**) The adjacent T5–10 intercostal arteries were dilated and tortuous. Their circuitous branches were radially distributed into the tumor body. As confirmed by surgery, the blood supply to the tumor was abundant. The tumor was removed piece by piece with extended excision of the partial pleura, aortic adventitia, and left pneumonectomy. Pathology revealed synovial sarcoma.

No intraoperative death occurred. Re-expansion of the pulmonary edema occurred in one case during surgery and was recovered by cardiotonic, diureticum, glucocorticoid, and prolonged mechanical ventilation. One patient underwent emergent surgery with complete resection and right pneumonectomy. Because of hemorrhagic shock and a rupture in the tumor body, image-guided transthoracic needle core biopsy was followed by emergent surgery. The patient died on the 15th postoperative day from cerebral hemorrhage, based on a clinical diagnosis. The pathology revealed a mixed germ cell tumor containing seminoma, embryonal carcinoma, and immature teratoma.

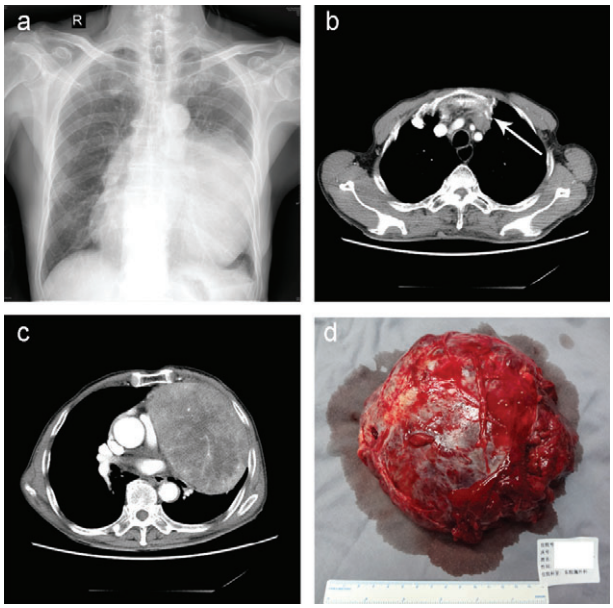

Figure 3 (**a**) A giant thoracic neoplasm was located in the left hemithorax. (**b**) An aberrant arterial branch originating from the internal mammary artery was distributed downward into the tumor body (see white arrow). (**c**) Large numbers of tortuous vessels were found within the tumor body in the arterial phase. The tumor was speculated to be solitary and completely encapsulated, with a wide-basement pedicle from the mediastinum. This speculation was confirmed by surgery. (**d**) The resected specimen measured 16.0 × 16.0 × 6.0 cm^3. Pathology revealed thymic carcinoid.

Pathological data

Pathological data are presented in Table 3. The most common pathological type was mesenchymal tumor (21 cases, 46.67%), including solitary fibrous tumor (7 cases), liposarcoma (6 cases), fibrosarcoma (2 cases), synovial sarcoma (3 cases), leiomyoma of esophagus (1 case), thymolipoma (1 case), and pleomorphic undifferentiated sarcoma (1 case). The second common pathological type was germ cell tumors (11 cases, 24.44%), including mature cystic teratoma (6 cases), seminoma (2 cases), yolk sac tumor (1 case), and mixed germ cell tumor (1 case).

Survival analyses

The median survival duration in all patients was 58 months (range 3–118). The one, three, and five-year survival rates were 86.0%, 64.4%, and 47.0%, respectively. Patients with tumors ≤20 cm at greatest diameter (n = 23) survived significantly longer than patients with larger tumors (n = 21) (median survival 73 vs. 41 months;

Table 2 Surgical data

Variables	Values
Surgical approach	
Median sternotomy	11 (24.44%)
Left posterolateral thoracotomy	14 (31.11%)
Right posterolateral thoracotomy	11 (24.44%)
Left anterolateral thoracotomy	4 (8.89%)
Right anterolateral thoracotomy	3 (6.67%)
T-shaped incision†	2 (4.45%)
Operation type	
Exploratory thoracotomy and biopsy	2‡
Palliative resection	4
Complete resection without extended resection	19
Complete resection with extended resection	20
Wedge resection of lung	5
Lobectomy or double-lobectomy	8
Pneumonectomy	3
Partial resection of the pericardium	11
Artificial vascular replacement of superior vena cava	3
Ligation and partial resection of the left venae brachiocephalica	4
Partial resection of sternum	1
Partial resection of diaphragm	2
Blood loss (mL)	1650 (20–13 000)
Volume of gross tumor (cm^3)§	2391 (320–13 808)
Weight of gross tumor (kg)	2.6 (0.9–6.0)

†T-shaped incision: Median sternotomy followed by anterolateral thoracotomy. ‡Postoperative histopathology showed fibrosarcoma and liposarcoma, respectively. §Volume = (length × $width^2$)/2.

Table 3 Pathological data

Pathological type	Values
Mesenchymal tumors	
Solitary fibrous tumor	7
Liposarcoma	6
Fibrosarcoma	2
Synovial sarcoma	3
Leiomyoma of esophagus	1
Thymolipoma	1
Pleomorphic undifferentiated sarcoma	1
Germ cell tumor	
Mature cystic teratoma	6
Seminoma	2
Yolk sac tumor	1
Mixed germ cell tumor	2
Thymic tumor	
Thymoma	2
Thymic squamous cell carcinoma	3
Thymic carcinoid	1
Rare malignant tumor of lung	
Pulmonary sarcomatoid carcinoma	2
Pulmonary blastoma	1
Immature teratoma	1
Lymphoma of mediastinum	
Non-Hodgkin lymphoma	3

$P = 0.033$) (Fig 4a). The median survival durations after exploratory thoracotomy, palliative resection, and complete resection with and without extended resection were 3, 15, 48, and 85 months, respectively ($P < 0.001$) (Fig 4b). Overall comparison showed that different resection status was closely correlated with prognosis. Pairwise comparison showed a better prognosis in patients who had undergone complete resection compared to patients who had undergone exploratory thoracotomy or palliative resection ($P < 0.001$ and $P = 0.004$, respectively). However, the difference between exploratory thoracotomy and palliative resection was not significant ($P = 0.107$). The difference between complete resection with and without extended resection was also not significant ($P = 0.157$).

Given the fact that there were only one or two patients with specific pathology types, we conducted survival analysis stratified by pathology group (Table 3). Overall comparison showed that pathology group was closely correlated with prognosis ($P = 0.001$) (Fig 4c). Pairwise comparison showed a better prognosis in patients with lymphoma and a poor prognosis in patients with rare malignant tumor of the lung. The difference between germ cell, mesenchymal, and thymic tumors was not significant.

Discussion

A giant thoracic neoplasm is extremely rare and has only occasionally been cited in the literature, usually in single cases.[7–25] To our knowledge, only one previous has reported conclusions after surgical treatment.[26] Our retrospective study of 45 patients showed the complexity and heterogeneity of giant thoracic neoplasm through clinical characteristics, imaging manifestations, surgical management, pathology, and prognosis. We also confirmed the effectiveness of CTA with 3D reconstruction imaging and biopsy pathology in the preoperative assessment for giant thoracic neoplasm.

The clinical characteristics of thoracic neoplasm vary because of slow and expansive growth. Large tumors >10 cm in diameter may cause symptoms such as chest tightness, shortness of breath, dyspnea, chest pain, cough, fever, and fatigue. In China, routine health examination is not available to the general public, particularly to poor farmers. Morbidity related to giant thoracic neoplasm in China is speculated to be higher than in developed countries.

Imaging manifestations are essential for radiologic diagnosis and preoperative assessment. Conventional contrast-enhanced CT is still the gold standard for the imaging evaluation of a giant thoracic neoplasm. However, clinical differential diagnosis between non-invasive and invasive tumors, as well as determination of the extent of local invasiveness, remains a challenge, even on CT scans. Thus, we

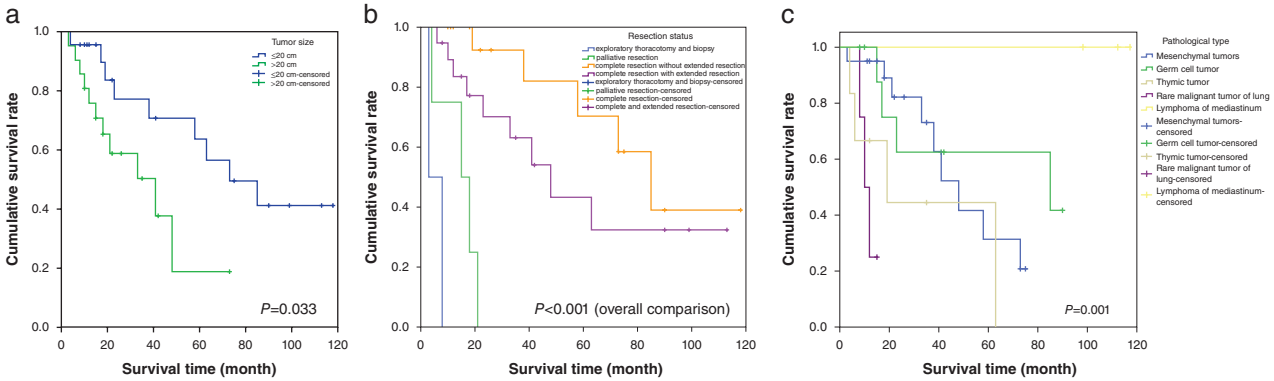

Figure 4 Kaplan–Meier survival curves for each single factor. (**a**) Patients with tumors ≤20 cm showed significantly better survival than patients with larger tumors (P = 0.033). (**b**) Survival was significantly different when stratified by tumor resection status (P < 0.001). (**c**) Pathology group was closely correlated with prognosis (P = 0.001).

introduced innovative CTA with 3D reconstruction imaging to selected patients with solid lesions abundant in blood supply or with a suspected unresectable mass. This procedure is not recommended if a cystic lesion or hypovascular tumor is strongly suspected, based on conventional CT scanning.

Contrast-enhanced CTA with 3D reconstruction imaging has been proven to better assess feeding vessels, local tumor expansion, and loco-regional invasion. It facilitates a more detailed preoperative assessment of surgical feasibility and safety.[6,27,28] This innovative imaging technique has the potential to improve stratification of patients for more tailored therapy and better outcomes.

In addition, intravoxel incoherent motion and diffusion magnetic resonance imaging, as well as fluorodeoxyglucose positron emission tomography, have great potential to distinguish between non-invasive and invasive tumors.[29] High-resolution superselective angiography has been widely applied in the diagnosis and treatment of vascular diseases, such as pulmonary arteriovenous malformation, gastrointestinal hemorrhage to perform both superselective angiography of the feeding artery, and embolization itself.[30] The practicability of these techniques for a giant thoracic neoplasm is worth studying.

Precise pathological diagnosis can be made by preoperative biopsy through image-guided transthoracic needle core biopsy or electronic bronchoscopy. The least invasive biopsy with the highest yield is preferred. Pathological results inform therapeutic decision and prognosis. The following correlations were concluded based on our study and experience. For benign or low-grade malignant giant thoracic tumor, such as thymoma, solitary fibrous tumor, and mature cystic teratoma, complete resection is always feasible and the prognosis is satisfactory. For giant soft tissue sarcoma, advanced thymic carcinoma, or malignant germ cell tumor, (especially an aggressive tumor with an abundant blood supply strongly suspected to be unresectable based on preoperative imaging manifestation), direct surgical treatment means a high possibility of conversion to debulking surgery or exploratory thoracotomy, increasing complication morbidity and poor prognosis. Therefore, neoadjuvant or even radical radiochemotherapy should be recommended for these selected patients prior to surgery.[31]

On the other hand, a biopsy adds time, cost, procedural risk, and the following limitations: (i) pathology based on small biopsies is not error free, and can be misleading – benign results do not exclude a malignant tumor; (ii) possibility of iatrogenic tumor cell dissemination and rupture of tumor body; and (iii) pneumothorax is the most common complication.[32] Preoperative biopsy is not obligatory for every giant thoracic neoplasm, but is recommended when an unresectable tumor is strongly suspected or non-surgical therapy is preferred based on clinical characteristics and imaging manifestations. It should be avoided for cystic lesions or resectable benign tumors.

Double lumen endotracheal intubation and intravenous anesthesia is recommended in order to prevent the occurrence of bronchial rupture and hemorrhage. In some cases, intubation in a semi-conscious state without the use of muscle relaxants followed by decisive thoracotomy is required to ensure safety.

Based on experience, the key to successful surgery is optimal surgical incision and approach, which determines whether a giant thoracic neoplasm can be sufficiently exposed and resected. Standard posterolateral thoracotomy and median sternotomy incisions are most commonly selected. An anterior lateral incision combined with a median sternotomy incision can be used for a patient with an anterior mediastinal tumor protruding to the unilateral or bilateral thoracic cavity. If the tumor is cystic or cystic-solid, a small incision in the cystic wall can be made to suck the cystic fluid, which not only avoids the spread of cystic fluid into the thoracic cavity, but also reduces

surgical difficulty. If the tumor is solid and completely encapsulated, direct complete resection of the tumor should be expected. If the tumor is excessively large and tightly adheres to adjacent tissues, careful separation along the inner surface of the tumor capsule can be performed. The tumor can be removed piece by piece in order to clearly expose the operating field under direct vision and improve surgical safety. There are always many feeding vessels, which should be ligated or sutured before resection. When using CTA with 3D reconstruction imaging, the tumor pedicle and feeding vessels should be located prior to surgery and handled with purpose during surgery. In cases involving the superior vena cava or innominate vein, angioplasty or prosthetic vessel replacement should be performed if necessary.

The definition of a giant thoracic neoplasm is mainly based on the location and volume of the neoplasm, regardless of the same pathological type or unified staging criteria. Obviously, a prognosis of benign or low-grade malignant giant thoracic tumor, such as thymoma, solitary fibrous tumor, and mature cystic teratoma, is promising. Outcomes of malignant tumors, such as giant soft tissue sarcoma, advanced thymic carcinoma, or malignant germ cell tumor is not satisfactory. However, an evaluation of the correlation between pathology, staging, and prognosis is unfeasible and useless. Except for pathology and staging, resection status is the most important prognostic factor in giant thoracic neoplasms, followed by tumor size. Radical surgery is the optimal therapeutic regimen for all resectable giant thoracic neoplasms, whether there is tumor invasion or not.

There are some limitations to our study. As a retrospective, single-center, database study, the results generated are dependent on the reliability of data collection and the study sample size. To minimize any bias, two independent investigators collected the data and an independent monitoring investigator audited data capture to minimize missing data and control concordance, as well as to include or exclude patients. Subgroup analysis stratified by pathology or staging was not possible because of the sample size and the low morbidity of specific pathological types.

In conclusion, because of its rarity and complexity, a giant thoracic neoplasm should preferably be treated in experienced centers for precise diagnosis and optimal therapy schemes with comprehensive consideration of clinical characters, imaging manifestations, pathology, surgical management, and prognosis. Innovative CTA with 3D reconstruction imaging together with preoperative biopsy are feasible and effective in therapeutic decision-making and surgical planning. Complete surgical resection remains the mainstay of curative therapy for all a priori resectable tumors with promising prognosis defined by imaging manifestations and preoperative biopsy. Further studies with larger multicenter cohorts, prospective clinical trials, and subgroup analysis stratified by pathology or staging are required to confirm these preliminary findings.

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Disclosure

No authors report any conflict of interest.

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