Individualized surgical treatment for patients with tumours of the cervicothoracic junction

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Abstract

OBJECTIVES: The cervicothoracic junction is a special section that connects the neck, thoracic cavity, mediastinum and axilla. Tumours in the region often invade or compress surrounding tissues and organs, which makes the surgical treatment difficult.

Key question
How does one select individualized surgical strategies for cervicothoracic junction tumours?

Key finding(s)
56% open surgery; 39% under VATS; 5% VATS with supraclavicular or posterolateral or hemi-clamshell incision.

Take-home message
VATS is widely used; comprehensive preoperative assessment and individualized approach during surgery enhance the prognosis.
METHODS: A retrospective analysis involving 69 patients with tumours at the cervicothoracic junction. Clinical data with regard to manifestation, surgical approach, resection degree, outcome and pathological types were collected.

RESULTS: A total of 48 cases of asymptomatic patients and 21 cases of patients with ≥1 clinical manifestation were enrolled in the study. Twenty-seven patients received radical resection with video-assisted thoracoscopic surgery. Anterior approach was the predominant treatment method in open surgery (25 cases, 36.2%), while the anterolateral approach was used in 8 cases (6 cases of hemiclamshell incisions and 2 cases of trap-door incisions). In addition, we observed 1 case of posterior approach, 2 cases of posterolateral approach and 1 case of supraclavicular approach combined with posterolateral approach. Pathological examination results revealed 67 cases of radical resection and 2 cases of microscopic residual. Neurilemmoma was the most widespread pathological type (30 cases, 43.5%), followed by tumour originating from fibrous tissues (5 cases, 7.2%). A 3-year overall survival rate of the 69 patients was 89.9%, while a 5-year overall survival rate was 85.5%.

CONCLUSIONS: Tumours associated with the cervicothoracic junction are characterized by their unique location, complex anatomy and various histopathological subtypes. An individualized approach during surgery enhances safety and standardized of treatments for patients with tumours located at the cervicothoracic junction.

Keywords: Tumours • Cervicothoracic junction • Surgical approach • Hemiclamshell

ABBREVIATIONS

3D Three-dimensional
MRI Magnetic resonance imaging
VATS Video-assisted thoracoscopic surgery

INTRODUCTION

The cervicothoracic junction, which is low in the front and high in the back, is a narrow region extending from the C7–T4 bilateral transverse processes to the first rib and the sternum [1]. The cervicothoracic junction can be defined as a transition zone from the neck with high mobility and lordosis to the rigid chest with kyphosis surrounded by bony structures [2]. The cervicothoracic junction is a special section that connects the neck and thoracic cavity, mediastinum and axilla. Based on anatomy, it includes the lower neck, thoracic inlet, superior mediastinum, upper thoracic cavity and the axillary region; that is, the region not only includes the vertical structures of the neck and chest but also the horizontal structures between the neck, chest and upper limbs, which implies that the adjacent structures, lesions and clinical manifestations in the area are very complex, and can be explained as follows. Firstly, because of the close association with key neurovascular structures in the region, tumours in the cervicothoracic junction frequently invade or compress surrounding tissues and organs, presenting certain technical problems [3]. Secondly, complete surgical resection requires multidisciplinary collaboration, including thoracic surgery, plastic surgery, vascular surgery and orthopaedics.

After Dartevelle et al. [4] proposed the anterior transcervicothoracic approach for the resection of lung cancer that has invaded the cervical structures of the thoracic inlet, and despite the advocacy for various alternative or improved approaches of the cervicothoracic junction including a combination of the anterior cervical approach with limited upper median sternotomy, none of the approaches have been standardized due to poor accessibility and visualization.

We retrospectively analysed the clinical data of 69 patients with cervicothoracic junction tumours who underwent surgery at our department from March 2008 to September 2020 and assessed the selected surgical methods and their efficacy to explore individualized surgical treatment strategies for cervicothoracic junction tumours and improve perioperative management.

METHODS

Ethical statement

Ethical approval was granted by the Ethics Committee of Zhongshan Hospital, Fudan University (Shanghai, China) (B2018-106).

Patient selection

The clinicopathological data of patients with cervicothoracic junction tumours who were admitted to the Department of Thoracic Surgery, Zhongshan Hospital of Fudan University (FDZSH) from March 2008 to September 2020 were retrospectively analysed. In the present study, patients were selected based on the following inclusion criteria: (i) computed tomography, computed tomography angiography or magnetic resonance imaging (MRI) were performed before operation, and clinical diagnosis was cervicothoracic junction tumour; (ii) patients received surgery at the Department of Thoracic Surgery, Zhongshan Hospital of Fudan University; and (iii) patients with complete clinical pathology data. Furthermore, we excluded patients if they satisfied any of the following criteria: (i) patients with impaired heart, lung, biochemical and coagulation functions, and were unable to tolerate surgery; and (ii) only endobronchial ultrasound-guided or needle biopsy was performed and clear pathology reports were obtained from our department.

Preoperative evaluation included assessment of the safety and effectiveness of the surgical procedure as follows. First, performing surgical safety assessments, such as such as laboratory tests, patient status scores and assessment of tolerance to anaesthesia and surgery. Second, evaluation of surgical procedure effectiveness, such as enhanced computed tomography examinations, MRI examination, computed tomography angiography, to evaluate the location, size and degree of tumour invasion. In the case of large tumours or a marked degree of external invasion, three-dimensional (3D) reconstruction of the tumour might be conducted to fully evaluate the possibility of complete resection (Fig. 1). Oncological assessments included assessment of the lymph nodes, blood metastases and preoperative pathology should be performed in our study. Moreover, evaluations including percutaneous needle biopsy under endobronchial
ultrasound-transbronchial needle aspiration can be used to verify pathological diagnosis before surgery.

Three-dimensional reconstruction

Patient-specific 3D reconstruction was performed for tumours at the cervicothoracic junction. Patients underwent enhanced computed tomography (Revolution CT, GE Healthcare, Milwaukee, WI, USA) and MRI scan, with slice thicknesses of 0.625 and 3 mm. Subsequently, the acquired data, in DICOM format, were imported into Materialise Mimics 23.0 and 3-Matic 15.0 software (Materialise NV, Leuven, Belgium), and segmentation, editing, registration and other rapid 3D reconstruction processes were implemented to reconstruct 3D digital models. After processing, the 3D reconstruction models were transformed into STereoLithography (STL) file format for preoperative planning and intraoperative navigation.

Survival analysis

Survival analyses were performed using IBM SPSS statistics software, version 22.0 (IBM, Inc., Armonk, NY, USA).

RESULTS

Baseline demographics and clinical characteristics

A total of 69 patients with cervicothoracic junction tumours were included in the present study. Among the patients, 33 were males and 36 were females; patients were aged between 15 and 74 years, with a median age of 49 years. Seventeen patients had chronic diseases such as hypertension, diabetes, supraventricular tachycardia and 23 patients were smokers, smoking 0.1–2.0 packs/day. The disease course of the patients was 0.2–108.0 months, with a median course of 9.0 months. The initial symptoms exhibited by patients varied; 48 cases (69.6%) were detected through asymptomatic examination and 21 cases (30.4%) exhibited more than one symptom. The most prevalent symptoms included chest tightness and numbness of the upper limbs or neck, which presented in 7 and 6 cases, respectively; the other symptoms were shoulder pain (3 cases), back pain (2 cases), difficulties with eating (3 cases) and hoarseness (2 cases). Furthermore, there was 1 case of Horner syndrome. The tumours in 39 patients (56.5%) were predominantly located on the left side of the mediastinum, while tumours in 27 patients were located on the right side, and 3 patients had tumours located in the middle mediastinum. Tumour sizes ranged between 2 cm ×
Table 1: Baseline characteristics of patients with cervicothoracic junction tumours

| Characteristics cases (%) |   |
|----------------------------|---|
| Sex, n (%)                 |   |
| Male                       | 33 (47.8) |
| Female                     | 36 (52.2) |
| Age, n (%)                 |   |
| <60 years                  | 53 (76.8) |
| ≥60 years                  | 16 (23.2) |
| Symptoms, n (%)            |   |
| Yes                        | 21 (31.4) |
| No                         | 48 (69.6) |
| Tumour size, n (%)         |   |
| <5 cm                      | 35 (50.7) |
| ≥5 cm                      | 34 (49.3) |
| Surgical procedures, n (%) |   |
| VATS                       | 27 (39.1) |
| Open surgery               | 37 (53.6) |
| VATS combined open surgery, n (%) | 5 (7.3) |
| Postoperative hospital days, n (%) |   |
| <7 days                    | 51 (73.9) |
| ≥7 days                    | 18 (26.1) |
| Resection, n (%)           |   |
| R0 resection               | 67 (97.1) |
| R1 resection               | 2 (2.9)  |
| Tumour origin, n (%)       |   |
| Neurogenic tumours         | 37 (53.6) |
| Non-neurogenic tumours     | 32 (46.4) |
| Nature of the tumour, n (%)|   |
| Benign                     | 50 (72.5) |
| Borderline/malignant       | 19 (27.5) |
| Complications, n (%)       |   |
| Yes                        | 7 (10.1)  |
| No                         | 62 (89.9) |

VATS: video-assisted thoracoscopic surgery.

Table 2: Postoperative pathology of patients with cervicothoracic junction tumours

| Postoperative pathology (n = 69) |   |
|----------------------------------|---|
| Neurogenic tumours, n (%)        | 37 (53.6) |
| Schwannomas                      | 30 (43.5%) |
| With haemorrhagic cystic degeneration | 2 |
| With mucinous degeneration       | 1 |
| Pseudoglandular schwannomas      | 1 |
| Other                            | 26 |
| Ganglioneuroma                    | 5 (7.2)  |
| Paraganglioma                     | 1 (1.4)  |
| Neurofibroma                      | 1 (1.4)  |
| Non-neurogenic tumours, n (%)    | 32 (46.4) |
| Fibrous tissue                    | 6 (8.7)  |
| Aggressive fibromatosis           | 5 |
| Non-aggressive fibromatosis       | 1 |
| Thyroid tissue                    | 5 (7.2)  |
| Thyroid follicular adenoma        | 2 |
| Subternal goitre                  | 1 |
| Thyroid papillary carcinoma       | 1 |
| Thyroid follicular carcinoma      | 1 |
| Lymphatic system                  | 5 (7.2)  |
| Diffuse T-cell lymphoma           | 1 |
| B-cell lymphoma                   | 1 |
| Lymphangiomia                     | 1 |
| Castleman disease                 | 1 |
| Lymphatic cyst                    | 1 |
| Other                             | 16 (23.2) |
| Metastatic malignant tumours      | 4 |
| Haemangioma                       | 2 |
| Lung adenocarcinoma               | 2 |
| Highly differentiated liposarcoma | 2 |
| Vascular tumour                   | 1 |
| Vascular endothelial tumour       | 1 |
| Sclerosing alveolar cell tumour   | 1 |
| Bronchial cyst                    | 1 |
| Thymoma                           | 1 |
| Myxoma                            | 1 |

1 cm and 25 cm × 22 cm. The general clinical data of the patients are presented in Table 1.

All patients were treated under general anaesthesia. The surgical procedures included 37 cases of open surgery, 27 cases of radical resection under video-assisted thoracoscopic surgery (VATS), 3 cases of VATS exploration combined with supraclavicular incision, 1 case of VATS exploration combined with posterolateral incision and 1 case of VATS exploration combined with hemiclamshell incision. The specific information about surgical approaches for tumours at cervicothoracic junction was exhibited in Supplementary Material, Table S1. In addition, postoperative pathology revealed 37 cases of neurogenic tumours and 32 cases of non-neurogenic tumours in the present study. Detailed information regarding postoperative pathology is presented in Table 2.

In the present study, we concluded that hemiclamshell (6 cases of hemiclamshell incisions) and trap-door (2 cases of trap-door incisions) incisions confer the following advantages [5, 6]: (i) scope of the resection is expanded to increase the possibility of achieving complete tumour resection; (ii) crucial structures including subclavian blood vessels, trachea, oesophagus, brachial plexus nerves, the vagus nerve and the phrenic nerve are fully exposed so that dissection of the subclavian blood vessels and the brachial plexus, angioplasty, reconstruction of blood vessels and neurolysis can be performed under direct vision; (iii) integrity of the sternoclavicular joint is preserved to reduce shoulder deformities and instability; (iv) the scope of rib resection and chest wall reconstruction are expanded; and (v) radical cure rate is enhanced by enabling clearance of the mediastinum and cervical lymph nodes.

Clinical outcomes

No perioperative death was observed in the present study and all patients were discharged from the hospital uneventfully. Postoperative hospital stay ranged between 2 and 62 days, with an average of $7.2 \pm 8.9$ days. Perioperative complication cases were 7 (10.1%), including 2 cases of hoarseness, 1 case of upper limb swelling, 1 case of upper limb numbness, 1 case of eyelid drooping, 1 case of chyle fistula and 1 case of fat liquefaction. Patients exhibiting hoarseness were treated with neurotrophic medicine, patients with chyle fistula received fasting and fluid infusion treatment, while patients with fat liquefaction were treated with routine dressing changes. All patients recovered gradually after receiving appropriate treatments.

In the present study, postoperative pathology revealed that complete resection (R0 resection) was performed in 67 patients (97.1%) and incomplete resection (R1 resection) was performed in 2 patients. The pathological results of patients who underwent
R1 resection revealed diffuse T-cell lymphoma and vascular endothelial tumours. We observed that the tumours of patients with T-cell lymphoma who underwent R1 resection were located at the cervicothoracic junction with no intact capsule, and the boundary with surrounding tissues was unclear. In addition, no swelling of the lymph nodes at the cervicothoracic junction was observed. We observed that the tumours of the other patients who underwent R1 resection grew along the subclavian artery with unclear margins. Notably, intraoperative frozen section pathology revealed that we achieved complete resection of vascular endothelial tumours while postoperative pathological diagnosis revealed incomplete resection. Moreover, 45 patients (65.2%) were followed up successfully and 24 patients dropped out. For benign lesions, the overall 3-year survival rate of patients was 100.0% and the overall 5-year survival rate was 89.5%. In contrast, the overall 3-year survival rate of malignant lesions was 54.5% and the overall 5-year survival rate was 36.3% (Fig. 2).

DISCUSSION

Three parts of the classic cervicothoracic junction, the front, middle and back, are separated by an attachment point of anterior and middle scalene muscles to the first rib [7, 8]. The anterior compartment, which is delimited anteriorly by the sternum and posteriorly by the attachment of anterior scalene muscle on the first rib, includes sternocleidomastoid and omohyoid muscles, subclavian and jugular veins, and scalene fat pad. In contrast, the posterior compartment is located behind the middle scalene muscle and contains posterior scalene muscle, posterior scapular artery, the stellate ganglion, sympathetic chain, long thoracic and accessory nerves, neural foramina and vertebral bodies. Furthermore, anatomical spaces between the anterior and middle scalene muscles are defined as the middle compartment with subclavian artery, phrenic nerve and trunks of the brachial plexus run through this region.

Tumours located at the cervicothoracic junction have various origins. The most widespread type of tumours in the present study were the neurological tumours (33 cases, accounting for 52.4%), including schwannomas, ganglion cell neuromas and paragangliomas, followed by tumours of the fibrous tissues, lymphatic system and metastatic tumours. Surgery is the first choice for surgically resectable tumours of the cervicothoracic junction. Performing fast-frozen section pathology during an operation is recommended to guide the intraoperative surgical plan and determine a comprehensive postoperative treatment strategy based on histopathological and molecular pathology tests.

Several surgical approaches have been developed for the operation of tumours in the region (Supplementary Material, Table S2). The choice of a surgical approach is a key factor influencing the feasibility of surgery, achievement of complete tumour resection and the occurrence of surgical complications. A supraclavicular incision should be considered when the tumour is located at the root of the neck with a complete capsule, as well as a smooth surface because it is convenient, safe and time-saving, without pronounced invasion of or adhesion to surrounding tissues. During surgery, a blunt dissection along the surface close to the mass may be performed to free the capsule and to completely remove the tumour, which prevents damage to the recurrent laryngeal nerve and thyroid. When the tumour is extensive and invades the thorax, as well as adheres to crucial structures such as blood vessels and nerves, it becomes extremely difficult to achieve enough exposure through a simple supraclavicular incision. Therefore, anterolateral approach or transcervical–thoracic incision should be used to avoid complications (rupture and bleeding of associated blood vessels, nerve damage, pneumothorax, etc.) In our study, most open-surgery cases were performed with anterior approaches since previous studies had reported anterior approaches facilitate exposure to critical neurovascular structures [9, 10]. There are various methods for the anterior approaches. However, different anterior approaches have different advantages and disadvantages and surgeons should choose most suitable approaches based on the patient’s situation. For example, although the transclavicular approach offers a superb view of the anterior, middle and posterior thoracic inlet, for patients who need to resect more than 3 ribs, the transclavicular approach might not be the best approach because it may result in a more troublesome postoperative course. On the other hand, the location of the lesions also plays an important role in determining the choice of surgical approach. For instance, Macchiarini et al. [10] had divided the cervical–thoracic junction into 5 areas and suggested the appropriate surgical strategy is generally chosen according to the locations of mass.

With regard to the protection of the surrounding crucial structures during separation and resection of the tumour (Fig. 3), our experience was as follows. First, based on blood vessels, separation of the proximal and distal end of the tumour invading the blood vessel can be conducted before placing the rubber thread and resecting the lesion. The occurrence of internal carotid occlusion and the integrity of the circle of Willis are essential preoperative evaluations for vertebral artery resection. Subclavian artery resection is more likely to lead to ischaemia of the affected limb and vascular replacement is required. Only a few tumours at the cervicothoracic junction invade the arteries such that vascular reconstruction is avoided by carefully dissecting the vascular and separating the tumour from normal tissues; protection of the thoracic duct is also critical, and careful separation and ligation could be considered when necessary to prevent chyloous leakage.
Second, with regard to the nerves, the recurrent laryngeal nerve should be protected when dissociating the neck region. The brachial plexus should be released carefully and preserved when the tumour is invading or oppressing the brachial plexus. Exposure of the nerve first may prevent nerve injury when separating tumours associated with the pre-vertebral fascia. Special attention should be paid to the protection of the phrenic nerve during surgery in the case of postoperative diaphragmatic paralysis and respiratory dysfunction resulting from phrenic nerve injury during costa resection or chest wall reconstruction.

Third, with regard to the ribs, chest wall reconstruction is not required when the upper 3 ribs are resected due to the occlusion of the scapula and clavicle. The chest wall should be actively reconstructed to avoid abnormal breathing when more ribs are removed and the chest wall is defective.

Fourth, regarding the vertebral body, if the tumour invades the vertebral body, a consultation with orthopaedist is required and MRI examination should be performed before the operation to fully determine the extent of invasion of the spine. Corpectomy and spinal decompression can considerably reduce the pain and paralysis caused by vertebral body destruction and spinal cord compression. Furthermore, if the tumour involves the epidural structure, corpectomy or laminectomy can be considered and the vertebral body can be reconstructed to achieve radical tumour resection. Adequate vertebral fixation should be performed in collaboration with orthopaedic surgeons to prevent spinal instability. Anatomical variations including vagal subclavian artery, absence of innominate veins and the double superior vena cava may occur in some cases. Preoperative stereoscopic 3D reconstruction facilitates the evaluation of the relationship between tumours and surrounding structures, which is helpful in fine anatomy and prevents injury during operation.

VATS technology is widely used to treat tumours located at the cervicothoracic junction. The present study included 27 cases (34.9%) of VATS radical resection, 3 cases of VATS combined with supraclavicular incision, 1 case of VATS exploration combined with posterolateral incision and 1 case of VATS exploration combined with hemiclamshell incision. Our findings suggest that VATS is a safe and reliable technique for the resection of tumours located at the cervicothoracic junction. During operation, VATS technology, which enables careful separation of tumours and surrounding structures, at the same time of finely haemostasis, confers unparalleled advantages in exposing fine structures (phrenic nerve, vagus nerve and stellate ganglion), in spite of its rare visual field and operating conditions. However, changing the position of the observation hole or adding an operation hole facilitates complete exposure for tumour removal. Overall, radical resection of tumours located at the cervicothoracic junction using VATS can considerably reduce surgical trauma and promote the recovery of patients.

VATS performs 4 major functions in the resection of tumours located at the cervicothoracic junction. First, diagnostic function: surgery using VATS approach can remove large tissue specimens to facilitate molecular pathology and diagnosis of tumours, and satisfy immunohistochemical requirements and gene detection simultaneously. Second, exploratory effect: VATS can be used to determine whether the tumour exhibits pleural dissemination, implantation metastasis, invasion of large blood vessels, vertebral bodies and other lesions; to determine the specific location of the tumour at the thoracic inlet, the extent of the chest wall or ribs involved, and the hilum or longitudinal intestinal lymph nodes. Third, assisted excision including dissection of hilar and mediastinal lymph nodes, separation of adherent lungs, and pulmonary lobectomy or sublobectomy can be performed routinely under VATS. Postural adjustment or conversion to open surgery is recommended for tumours that are too extensive to be completely removed under the endoscope after the procedure is completed, which not only ensures that the tumour is not removed until it is completely isolated but also prevents blind expansion of the incision and reduces surgical trauma. VATS conducted through an incision in adjacent spatiun intercostale or 5 cm away from the associated chest wall can be used to determine the extent of involvement of the costa, chest wall or vertebral bodies to avoid excessive resection of the costa and chest wall, in turn, reducing the risk of developing flail chest, pterygoid shoulder and shoulder strap injury. Fourth, radical resection: radical resection under VATS can be performed in patients having tumours with complete capsules, which can be completely separated under an endoscope; that is, tumours located in the periphery of the lung with no invasion of the surrounding structures.

The development of modern oncological technologies has promoted the treatment of tumours of the cervicothoracic
junction. Preoperative neoadjuvant therapy also provides an opportunity to achieve complete tumour resection. Surgeons should strictly regulate indications and opportunities for surgery and enhance comprehensive preoperative assessment of tumours located at the cervicothoracic junction. Selecting an appropriate surgical approach based on the condition of a patient and adopting individualized surgical treatment strategies will help improve the prognosis of patients and enhance the quality of life after surgery.

SUPPLEMENTARY MATERIAL

Supplementary material is available at ICVTS online.

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Author contributions

Shuai Wang: Conceptualization; Data curation; Writing—original draft. Zhencong Chen: Conceptualization; Data curation; Formal analysis; Writing—original draft. Ke Zhang: Investigation; Validation. Lijie Tan: Funding acquisition; Validation. Fazhi Qi: Data curation; Resources. Yong Zhang: Data curation; Investigation; Methodology. Ting Zhu: Data curation; Investigation; Resources. Zenggan Chen: Data curation; Resources; Validation. Qun Wang: Funding acquisition; Resources; Supervision. Wei Jiang: Conceptualization; Funding acquisition; Writing—review & editing.

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