Evaluating Transcervical Lymphadenectomy in Systematic Diagnosis of Lung Cancer

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Abstract: Background: The study of mediastinal lymph node metastasis in patients with lung cancer is very important to formulate treatment strategies.

Objective: To explore the value of transcervical lymphadenectomy in the systematic diagnosis of lung cancer.

Methods: Transcervical lymphadenectomy was used as part of the systematic diagnosis of lung cancer in Hospital Universitario Manuel Ascunce Domenech in Camagüey. The universe consisted of 346 patients and the sample was a simple random probability type, consisting of 65 patients.

Results: It was mainly male, over 60 years old. The most common histological type is adenocarcinoma, and the upper lobe is the most affected. A total of 205 lymph nodes were resected, most of which were positive and histologically negative, mainly in lymph nodes less than 1 cm diagnosed by CT. Staging metastasis existed in clinicopathological correlation, and the sensitivity and specificity of the study sample were 100%. There are few complications.

Conclusion: Transcervical lymphadenectomy is an effective method for the diagnosis of lung cancer and mediastinal lymph node metastasis.

Keywords: Lung neoplasms/surgery, Lung neoplasms/complications, Lung neoplasms/imaging diagnosis, Lymph node resection/method, Longitudinal study

1. Introduction

Lung cancer is the most common tumor in the respiratory system and the tumor with the largest death toll among all cancers, making it a serious public health problem[12]. Despite significant progress in diagnosis and staging techniques and the widespread use of chemotherapy and radiotherapy in treatment, the five-year survival rate (15% at all stages) remains low[3].

According to the American Joint Commission on Cancer (AJCC), the clinical or preoperative staging (cTNM) of CP refers to the use of all available means before treatment, including invasive examination. If this is correct, the rate of exploratory thoracotomy and incomplete resection should not exceed 8%–10%[4,6]. Pathological staging (pTNM) is based on macroscopic and microscopic examination results of tumors and other tissues[4].

An ideal CP staging technique should be feasible, with repeatability of results, safety, high sensitivity and negative predictive value, as well as simple and effective cost[7].

The lymph node assessment of CP stems from the need to determine
the tumor range in different lymph node seasons, which is essential for dividing lymph nodes into N0, N1, N2 and N3, which is the basis of staging\[3\]. For this purpose, various technologies have been designed, many of which are video assisted.

In 2005, transcervical extended mediastinal lymphadenectomy (TEMLA) was established in Poland. This technique was described by Kuzdzal cited by Yendamuri et al.\[8\]. It allows resection of all mediastinal ganglion lesions, except for pulmonary ligament lesions (ganglion station No. 9). The main indication is the staging of operable patients with bronchial lung cancer. It has been modified and improved to achieve pneumonectomy and lymphadenectomy at No. 9 lymph node station.

A few years later, the Polish group\[9\] published a prospective randomized clinical trial to compare the diagnostic accuracy of TEMLA with traditional mediastinoscopy. Due to the significant difference in false negative results between the two techniques (5 vs 0, \( P = 0.019 \)), this work was completed in only 82 patients. The sensitivity and negative predictive value of mediastinoscopy were 37.5% and 66.7%, respectively. However, both values were in the group of patients receiving TEMLA.

The operation was performed by a 5 to 8 cm transverse cervical incision. With the help of a special sternal retractor, the sternum can be raised, allowing extensive surgery throughout the mediastinum. Most operations are performed with open surgical instruments, while the anatomy and resection of underwater (No. 7) and paraoesophageal (No. 8) gland lesions are performed through video mediastinoscopy, and the subaortic (No. 5) and para-aortic (No. 6) gland lesions are performed with the help of video-assisted thoracoscopy or through extended video mediastinoscopy\[8\].

As part of the diagnostic system for CP patients, the first part of the above technology was carried out at Hospital Universitario Manuel Ascunce Domenech in Camagüey. This technology allows histopathological study of the upper ganglion, combined with the anterior mediastinotomy of Mc Neil and Chamberlain cited by Zielinski\[10\]; when the aortic area is involved, according to the map of the International Association for the Study of Lung Cancer (IASLC)\[11\].

2. Methods

From September 2015 to December 2018, a prospective longitudinal analysis was conducted on patients undergoing cervical lymphadenectomy in the Department of general surgery of Hospital Universitario Manuel Ascunce Domenech in Camagüey.

There were 346 patients. The simple random probability sample included 65 patients, with the pathological staging (pTNM) in the 7th edition of IASLC\[10\] as the dependent variable and age, gender, tumor type, lymph node area and size, clinical stage, predictive value, sensitivity, specificity and comorbidity as the independent variables.

The inclusion criteria were: patients diagnosed with CP who underwent transcervical lymphadenectomy and participated in the study with informed consent during the study; while the exclusion criteria were patients who could not complete the data contained in the table. The calculation security of sample size is 95%, the accuracy is 3%, the proportion is 5%, and the expected loss rate is 15%.

Patients with CP and lymph node involvement diagnosed by CT were treated with transcervical lymphadenectomy. The database is established through a table that allows the collection of clinical history data in SPSS 25 for windows professional statistics package and the application of exploratory and confirmatory statistics. The table of one variable uses descriptive (exploratory) statistics, uses the total number and 100%, and two or more variables use Mc Nemar correlation coefficient and test to calculate the proportional hypothesis test and chi-square test of qualitative variables. The results are displayed in the chart created for this purpose.

3. Ethics

This is a study to evaluate the application of transcervical lymphadenectomy in the diagnosis of non-experimental PC. Before proceeding the study, the informed consent form should be signed by patients and their families to respect the integrity and well-being of patients.

4. Results

The average age was 60.93 years old, and men accounted for 70.7%. Among non-small cell tumors, adenocarcinoma accounted for 38.4%, followed by epidermoid carcinoma and large cell carcinoma, accounting for 20% and 3.07% respectively.

The most common site was the upper lobe, with the right lobe accounting for 56.9%. The most common clinical stage was IIIA, accounting for 78.4%. A total of 205 lymph nodes were studied, with an average of 3.31 lymph nodes per patient, the largest 9 and the smallest 1, of which 129 were positive, 62.9% and 76 were negative, 37.01%. 53.8% of the subjects had only one affected season (Table 1).
Table 1. Characteristics of transcervical lymphadenectomy

| Variable                      | Result                      |
|-------------------------------|-----------------------------|
| Age                           | Average: 60.93              |
|                               | Maximum: 84                 |
|                               | Minimum: 36                 |
| Gender                        | 46 (70.7%)                  |
| 1. Male                       |                             |
| 2. Female                     | 19 (29.3%)                  |
| Tumor type                    | 18 (27.6%)                  |
| 1. Non small cell             |                             |
| 1.1 Adenocarcinoma            | 25 (38.4%)                  |
| 1.2 Epidermitis               | 13 (20%)                    |
| 1.3 Large cell                | 2 (3.07%)                   |
| 2. Small cell                 | 7 (10.7%)                   |
| Anatomical localization of lung tumors |                   |
| 1. Right upper lobe           | 37 (56.9%)                  |
| 2. Middle lobe                | 2 (3.07%)                   |
| 3. Left superior lobe         | 11 (16.9%)                  |
| 4. Right lower lobe           | 10 (15.3%)                  |
| 5. Left lower lobe            | 5 (7.6%)                    |
| Clinical stages               | 51 (78.4%)                  |
| 1. III A                      | 14 (21.6%)                  |
| 2. III B                      |                             |
| CT study of lymph nodes       | 3.31                        |
| Average value                 |                             |
| Maximum                       | 9                           |
| Minimum value                 | 1                           |
| (a) Positive                  | 129 (62.9%)                 |
| (b) Negative                  | 76 (37.01%)                 |
| Total                         | 205 (100%)                  |
| Number of stations (number of patients) | 35 (53.8%) |
| 1) Single station             |                             |
| 2) Multi station              | 30 (46.2%)                  |

Source: form

According to the lymph node map of IASLC, the upper lymph node area was studied by cervical lymph node resection. The highest positive rate was the upper paratracheal ganglion (right and left), 73% and 31% respectively, followed by the lower paratracheal ganglion on both sides. For the aortic region, the positive rates of stations 5 and 6 were 16% and 15%, 12.4% and 11.6%, respectively (Table 2).

In the relationship between lymph node size and histopathological results, lymph nodes less than 1 cm were mainly negative, which was statistically significant compared with lymph nodes greater than 1 cm (P < 0.05) (Table 3).

According to the correlation between preoperative CT clinical stage and the results of transcervical lymphadenectomy, 10 patients with newly treated IIIA (2 cases and 17.6%) metastasized to stage I and II (2 cases and 17.6%). 74.5% of the patients were still in phase IIIB, and 3 cases (5.8%) entered phase IIIB. Among the patients initially diagnosed with IIIB, one patient (7.1%) entered phase II, six patients (42.8%) entered phase IIIA, and seven patients (50%) were still in phase II. However, in the analysis of 38 patients with stage IIIA (excision and standard lymphadenectomy were performed), only 7 (53%) patients retained the stage, and 1 (2%) and 10 (19.6%) patients transferred from stage I and II to early stage, respectively (Table 4).
### Table 2. Number of lymph nodes resected according to lymph node zones

| Ganglion area                  | Number of lymph nodes | Positive  | Negative | Significance P |
|--------------------------------|-----------------------|-----------|----------|----------------|
| 1. Supraclavicular region      | N = 205               | 19 (8.7%) | 17 (22.3%)| P < 0.05       |
| Upper area                     |                       |           |          |                |
| 2. Upper air pipe              |                       |           |          | P < 0.05       |
| 2R. Right                      | 35 (36.9%)            | 49 (40.5%)| 24 (31.5%)|                |
| 2L. Left                       | 31 (15.1%)            | 16 (12.4%)| 13 (17.1%)|                |
| 3a. Prevascular                | 2 (1.5%)              |           |          |                |
| 3p. Retrotracheal              | 0                     |           |          |                |
| 4. For lower tracheal          |                       |           |          |                |
| 4R. Right                      | 33 (16.9%)            | 21 (16.2%)| 12 (15.7%)| P < 0.05       |
| 4L. Left                       | 12 (5.8%)             | 9 (7%)    | 3 (4%)   |                |

### Pulmonary aortic region*

|                     | Positive  | Negative | Significance P |
|---------------------|-----------|----------|----------------|
| 5. Subaortic        | 21 (10.2%)| 16 (12.4%)| P < 0.05       |
| 6. Aortic           | 17 (8.2%) | 15 (11.6%)|                |

*This area was scanned in conjunction with McNeil and Chamberlain’s anterior mediastinotomy. Source: form.

### Table 3. Correlation between CT axial scanning ganglion size and histological results

| Section size | Histopathological results  | P |
|--------------|-----------------------------|---|
| 1. <1 cm     | Positive 75 (36.5%)         | P < 0.05 |
|              | Negative 54 (26.3%)         |    |
| 2. >1 cm     | Positive 25 (12.1%)         | P < 0.05 |
|              | Negative 51 (24.8%)         |    |

Source: form.

### Table 4. Correlation between preoperative and postoperative histology of lymph nodes

| Preoperative clinical staging | Preoperative clinical staging | Postoperative pathological staging | P   |
|-------------------------------|------------------------------|-----------------------------------|-----|
| III A (51)                    | Phase I                      | 1 (2%)                            | 1 (2%) | P < 0.05 |
|                               | Phase II                     | 9 (17.6%)                         | 10 (19.6%) |
|                               | Phase III A                  | 38 (74.5%)                        | 27 (53%) | P < 0.05 |
|                               | Phase III B                  | 3 (5.8%)                          | 0 |

| III B (14)                    | Phase I                      | 0                                 | 0 |
|                               | Phase II                     | 1 (7.1%)                          | 0 |
|                               | Phase III A                  | 6 (42.8%)                         | 0 |
|                               | Phase III B                  | 7 (50%)                           | 0 |

Source: form.
When analyzing the positive and negative predictive values and sensitivity and specificity of transcervical lymphadenectomy as part of pathological staging, although this is a supplement, there is an advantage in 100% specificity and sensitivity in the series studied (Figure 1).

There were few complications in this series, which was 1.6%. There was no mortality in the study series (Table 5).

![Figure 1. Predictive value of transcervical lymphadenectomy as a diagnostic procedure for mediastinal ganglion research.](image)

*Negative predictive value  
**Positive predictive value

| Complication                  | Number (%) |
|-------------------------------|------------|
| Recurrent paralysis           | 1 (1.5)    |
| Wound infection               | 1 (1.5)    |
| Wound granuloma               | 2 (3.07)   |
| Total                         | 4 (6.1)    |

Source: form.

5. Discussion

CP accounts for 13% of all cancer diagnoses and 20% of cancer deaths. The diagnosis age of most cases is between 55 and 75 years old, and the peak is between 65 and 70 years old. Non-small cell type accounts for 80%, which can be divided into several histological forms according to frequency\[^{1,2}\]: adenocarcinoma (20%–45%), squamous cell carcinoma (25%–40%) and large cell carcinoma (15%–20%), were consistent with the study series.

CT is the first examination commonly used in mediastinal lymph node staging (clinical staging)\[^{11,12}\], in which the adenosis is more than cm in size on the small axis is considered pathological, with a sensitivity of 60% and a specificity of 60%–80%. However, according to the literature on this subject, 40% of cm large lymph nodes will not metastasize and 10%–15% of cm small lymph nodes will be affected in histopathological studies, which is consistent with the results of the study\[^{11-13}\].

Prospective studies showed that surgeons could not determine the involvement of lymph nodes in CP without biopsy\[^{14,15}\]. In these prospective studies, the visual and palpation results of lymph nodes during thoracotomy were related to the results of histological examination, because without histological analysis, the sensitivity was 71% and the positive predictive value was 64%. Although there are a large number of reports on this subject in the literature, there is still no consensus on the scope of lymphadenectomy and the long-term prognosis at the time of treatment, but not at the time of diagnosis\[^{16,17}\].

With the passage of time and the increase of information, people have a better understanding of the anatomical basis of pulmonary lymphatic drainage mode, which has led to the development of more accurate indications for selecting more selective lymphadenectomy when performing CP radical surgery or using invasive methods in staging\[^{11}\]. However, positron emission tomography (PET), as supplementary
evidence of mediastinal lymph node staging, has a negative predictive value (VPN) between 93% and 96%\cite{17}.

That is, in 95% of PTE, mediastinal adenosis has no tumor, which is correct\cite{15}. The positive predictive value was slightly lower (85%). Therefore, to summarize: it is important to know whether mediastinal lymph nodes have metastasis originating from CP, which depends on whether the treatment strategy is completely different, if before N1 (surgery), N2 (preoperative induction and reassessment chemotherapy, or primary resection and lymphadenectomy with minimal N2, as in some cases in the series) or N3 (chemotherapy and radiotherapy). It is generally believed in the literature that the clinical staging of CT and PET is 100% reliable in the state of mediastinal ganglion, which provides a reason for invasive surgery\cite{18,19}.

The stage III A\cite{10} is a locally advanced stage. Generally, patients visit late, and clinical CT examination usually needs preoperative biopsy for verification. For some schools, surgery is not allowed, but for other schools, when the disease is very small (one station), they will undergo surgery. If the patient’s condition permits, the first operation group (as described in the series) has only one group of affected lymph nodes (except the seventh station), with lymph nodes <3 cm and no extracystic infiltration or bulky lymph nodes, while the other groups will do so even if there is more than one affected group, but the lymph nodes of patients with N1 affected III A at the tenth station are <3 cm\cite{20,22}.

These considerations led some working groups to perform invasive examinations, including mediastinoscopy or hypermediastinoscopy, depending on the presence of 100% of bronchial cancer, in order to histologically confirm the invasion of mediastinal lymph nodes, of course, as long as there is technology. A preliminary series by Zielinski M et al.\cite{23} in 83 TEMLA operations, they described an average of 32.8 surgically resected adenopathy (terminal 8–77), with sensitivity and negative predictive value of 96.2% and 99.6%, respectively.

However, most\cite{23,24} performed mediastinoscopy or mediastinotomy in the following cases: if CT was performed only when the adenosis was more than cm. Below 1 cm, they think they are not affected\cite{24}. Micrometastasis occurs in only 10% of small-scale adenocarcinoma, which also represents the N2 subgroup with better prognosis. When mediastinal PET is positive, lymph nodes involvement also needs to be confirmed histologically by mediastinoscopy or mediastinotomy. Patients with negative PET (95% of VPN) can undergo thoracotomy directly.

In 1985, Feinstein AR, cited by López Encuentra et al.\cite{25}, described the Will-Rogers phenomenon in PC as a predicted migration of the same PC stage that may occur when more sensitive staging diagnostic methods are used in different time periods. The Union for International Cancer Control (UICC) has established a deterministic factor (factor C) to evaluate the grading safety of tumor staging. At the stage of clinical staging, the possibility of classification deviation of cT, cN and cM varies\cite{26}.

In the stage of pathology and surgery, the biggest problem is the evaluation of pN0. For the pN0 category, it is necessary to develop criteria to achieve this classification at an appropriate level of certainty. Just as changes in technology and standards may cause staging migration problems in cancer staging systems. As a hypothesis, when applying more stringent classification certainty criteria, there may be digital migration of cases between categories and stages. In addition, if an increase in survival is observed, these changes may have an impact on prognostic migration, the Will-Rogers effect\cite{25,27}.

The incidence of transcervical lymphadenectomy reported in all series was low, ranging from 6% to 7%, which was consistent with the results. However, this is a high-risk process, due to the complexity of the anatomical structure of the region, an important learning curve is required. Surgical accidents, especially those related to vascular structure, may be fatal\cite{9}.

6. Conclusion

Transcervical lymphadenectomy is helpful to the histopathological analysis of upper lymph nodes and is an auxiliary diagnostic tool for CP patients. It can formulate treatment strategies by showing high specificity and sensitivity and minimal complications, especially in hospitals without advanced technology, such as specific video endoscopy technology.

Conflicts of interest

The authors declare that they have no conflict of interest.

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