Possibilities of Computer Assisted Tomography (CT) in Evaluation of Lung Cancer Operability

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SUMMARY
As is well known, surgical treatment is the most effective therapy for non-small cell lung cancer, although only a small number of patients are suitable for this type of treatment (25%-30%). The outcome of operative treatment and prognosis greatly depends on accurate preoperative diagnostic process using the TNM classification. Until now, different diagnostic methods are used in the preoperative staging of this severe illness, including computer assisted tomography which acquired a leading role. Despite its high value as a method of assessing the operability of lung cancer, there is a smaller percentage of diagnostic oversights where the stage was under or over-estimated and where discrepancy between CT and operative findings was present. Prospective study was conducted on 60 patients with lung cancer in the period from December 2000 to December 2007. Among our respondents there were more males (6.5:1), average age was 56; the youngest patient was 32 and the oldest 70 years olf. All patients underwent complete pulmonary and bronchial CT examination and then were subjected to one of the surgeries (28 lobectomies, 15 pneumectomy and 17 exploration thoracotomy) with pathohistological verification of findings. CT and postoperative lung cancer results were compared and statistically processed to one of the surgeries (28 lobectomies, 15 pneumectomy and 17 exploration thoracotomy) with pathohistological verification of findings. CT and postoperative lung cancer results were compared and statistically processed using the usual statistical methods. The results show that CT as a method in the preoperative clinical evaluation of patients with lung cancer is very useful because of its high diagnostic accuracy in determination of TNM stages of disease (83.33% accuracy, sensitivity 76.40%, specificity 93.00%, PPV 90.90% and 81.25% NPV). CT of thoracic organs still remains irreplaceable method in everyday clinical treatment of patients with lung cancer.

Keywords: CT, TNM, staging, surgical treatment

1. INTRODUCTION

While in the early years of twentieth century world literature described 374 cases of lung cancer today in the European Union is detected 270 000 cases annually, and over 330 000 people dies (incidence of 21%, mortality 29%) (88). Lung cancer is the leading cause of death in the United States, with approximately 170 000 deaths per year, of which three quarters were men, and the fourth woman (1).

For the past ten years there is a noticeable increase in the incidence in women (about 4%), which is explained by the increasing frequency of smoking habit in this population. (2) Characteristics of bronchial cancer disease in becoming mass in so called “vulnerable group”, consisting of men over 40 years of age, especially with smokers of 20 or more cigarettes per day (3).

Because the incidence rate and mortality are very close it is obvious that in the past few decades, little progress has been made in terms of prevention, early detection and treatment of this malignant disease. Prognosis of patients with bronchial cancer is still poor because there is only 10-15% chance of 5 years survival after diagnosis (4).

The disease usually occurs between 55 and 65 years of age, although it is not rare even in younger or older.

It is calculated that the four main types are in 90-95% of cases primary malignant lung cancer: squamous cell, adenocarcinoma, large cell carcinoma and small cell cancer. The biological behavior of lung cancer is related to the cellular type and the degree of its differentiation (and therefore exist different sub types) (2).

The purpose of staging is to determine the extent of disease for the selection of patients who will benefit from surgery, because only thoracotomy with complete tumor resection gives a satisfactory result (3).

In assessing the local extension of tumor, lymph nodes affection and presence of distant metastasis in non small cell tumors used is TNM classification, however, with this assessment is necessary to know whether it was made on the basis of clinical diagnostic staging (cTNM), or postoperative histological staging (pTNM).

Clinical diagnosis involves diagnostic assessment of all anamnestic information which include: patient history, physical examination, various radiological diagnosis results (standard radiography, tomography, CT, MRI, DSA of pulmonary artery, aspiration percutaneous biopsy under CT control, and recently PET), then the endoscopic methods and other results which may show extra thoracic metastases (US, scintigraphy) (4,5).

Before the discovery of a CT, extent of cancer was mainly determined with classical chest X-rays and invasive above mentioned methods which are in fact small surgeries and cannot be applied in all patients (6).

Computerized tomography (CT) is today one of the major imaging methods, and the method of choice in the evaluation of clinical diagnostic assessment of lung cancer (7).

Today is more and more accepted schematic map of lymph nodes (American Society Lymph node Map) recommended by the American Thoracic Society (ATS) (8), which describes all the possible positions of lymph nodes in the mediastinum and hilar regions. Tumors in stage I is limited to the lungs, without expanding in pleura without lymph node and distant metastases.

Stage II is divided into IIA and IIB, depending on whether the tumor stage is T1, T2 and T3. Tumors of stage II (T1N0M0) are the same as stage Ia, but with metastases to ipsilateral peribronchial and/or hilar lymph nodes as re-

**Figure 1.** CT scan of the apical right tumor size of 3cm which is in contact with the chest wall without infiltration – T3 stage (Pancoas tumor).
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stage IIb includes stage T1 tumors with ipsilateral, peribronchial or hilar nodal metastases (N1), and T1-T3 tumors cannot be surgically resected with ipsilateral mediastinal and/or subcarinal lymph nodes (N2).

Stage IIB tumors affect the vital mediastinal structures such as large blood vessels or esophagus (T4), or spread to contra lateral mediastinal or hilar lymph nodes (N3). Stage IV disease with distant metastases.

The most effective treatment of non small cell lung cancer is surgical, and it is possible for tumors whose staging matches stage I, II and IIIa disease, while tumors in stage IIB and stage IV cannot be surgically removed. Surgery may be radical or palliative.

In case of tumor stage I and II standard surgery is segmentectomy, lobectomy or pneumectomy depending on the size and localization of tumors, and in case of patients who refuse surgery or are inoperable for other contraindications (cardiovascular, respiratory insufficiency) which receives curative radiotherapy. The results are worse than after surgical resection. Five-year survival is between 17-32%.

It also may include adjuvant chemotherapy, but it does not improve the results. The difference between stages II and IIIa is important for patients because it represents the transition between the conventional surgical approach and more extensive tumor and lymph nodes resection. Stage IIIa means technically feasible resection despite progressed disease, because they have the benefit of tumor and lymph nodes resection (longer survival of patients). Five-year survival after resection of T3 or N2 stage is 22.2%, with postoperative mortality rate 6.7% (9).

2. GOAL
The main goal of our research is to analyze the possibilities of CT in evaluation of non small cell lung cancer (NSCL) operability.

3. MATERIAL AND METHODOLOGY
In the period from December 2000–December 2007 presurgically is processed 60 patients with CT examination in patients who had previously been hospitalized at the clinic Podhrastovi, where in addition to CT is made a complete treatment of patients and where the material was taken for histological analysis so that the diagnosis of lung cancer was confirmed in one or more ways: analysis of bronchial swab “brush biopsy”, catheter aspiration of sediment or transthoracic biopsy under CT control, and histological analysis of biopsy sample material taken during bronchoscopy. Thereafter, all patients were operated on the Thoracic Surgery of the Clinical Center in Sarajevo. Data collected for needs of our research, are: age, gender, the findings of the standard chest x-ray, bronchoscopy finding, CITO analysis findings.

result intrapulmonary expansion of the primary tumor.

Stage IIB includes stage T1 tumors with ipsilateral, peribronchial or hilar nodal metastases (N1), and T3 tumors, which directly affect the chest wall, diaphragm, mediastinal pleura, parietal parenchyma without nodal (N0) and distal (M0) metastases.

Stage II includes tumors and spread to
or CT pointed to infiltration of pulmonary artery, which was not confirmed surgically. At 4 (10.8%) patients, there was a false negative finding on the basis of CT, and there was contact with the infiltration (in 2 cases, pulmonary artery, pulmonary vein in one, and one superior vena cava) (Graph 2).

Based on the obtained data we can conclude that the contact of tumor with mediastinal structures gives sensitivity of the method in 73.3%, specificity 90.9 accuracy of 83%, PPV 84.61% and 83.33% NPV.

After surgery, the tumor that had contact with chest wall of the 14 patients, for 7 patients contact was less than 3cm, and no infiltration was found. At 5 patients with tumors of contact longer than 3 cm and less than 5 cm, with 3 patients infiltration is not found, while in 2 patients there was infiltration of the chest wall (which is estimated CT). With 2 patients the contact was more than 5 cm, and due to infiltration and extent of the process it is evaluated as inoperable.

When compare CT and operative findings we found 13 truly positive (inoperable), and 40 truly negative (operable), 4 false negative (CT operable) and 3 false positive (CT inoperable) (Graph 3). These results determine the sensitivity of the CT method of 76.40%, specificity 93.0%, accuracy 88.33%, PPV 90.90% and 81.25% NPV.

Based on the results we see that the accuracy of CT in the I, IIA and stage IV of the disease was 100%, 86% IIb, IIIa in 70%, stage IIIb IN 87%, and the least accuracy of tumor in stage Ia, and IIIa IIb ($X^2$ = 93.557 P = 0.0001 ) (Graph 4).

Stage IIIa and IIIb are often diagnostic problem, so in addition to CT we should include other diagnostic methods, or have surgery (exploration thoracotomy) to demonstrate operability of the process.

5. DISCUSSION

Previous international experiences indicate that after diagnosis of lung cancer and disease staging about two-thirds of patients with non small cell lung cancer are usually already in inoperable stage (IIIB and IV), while for 10% this is determined during the thoracotomy. According to this it can be concluded that only 25% of patients may be subjected to radical surgical procedure for permanent cure. Considering all cases of non small cell lung cancer, regardless of their treatment, the average five-year survival by stage of disease is: I in about 50%; II 30%; IIIa 15%; IIIB <5% and IV <1% (10). Favorable outcome is in stage I and II disease, depending on the pathohistological type of tumor (better in squamous cell then adenocarcinoma), ranging from 52 to 83% (11). The percentage of survival in case of adenocarcinoma after complete resection is 52 to 83% in stage I and II, and stage III 21 to 35%, while at the same stage of planocellular type is between 37 and 46% (12).

Computerized tomography (CT) allowed much clearer detection of the primary tumor, plus hilar and mediastinal lymph nodes, pleura, chest wall and vascular structures. The method has proved very useful in the planning, implementation and monitoring of the effects of surgical, radio and chemotherapy, making treatment scheme, better determination of size and determination of tumor volume and reduced normal tissue ionization. We have to mention the main drawbacks and limits of this method. It is well known that CT is ionizing method that often results in additional costs, so there are limits in accurate determination of lung cancer stage. Imperfect criterion for “normal” lymph node with CT makes measuring their size difficult (short axis up to 1 cm) which is the cause of false negative and false positive findings, smoking, CT findings of thoracic organs, and additional diagnostic tests, CT of the spine, MR of thoracic organs DSA of pulmonary artery, abdomen US, skeletal scintigraphy and surgeon remarks.

All examinations were made on the apparatus Somatom Volume Zoom from “Siemens” in suprimation position of a patient which uses 4 rows of detectors and can be used as 1mm detectors (4x1), 2.5 mm detectors (4x2.5) or 5 mm detectors (4x5). Depending on the choice of parameters scans can be reconstructed in 3D reconstructions after scanning.

4. RESULTS

All patients (total 60) who underwent CT or thoracic organs were subjected to surgery. Made are 15 pneumonectomies, 28 lobectomies and 17 explorative thoracotomy (Graph 1). Contact with macro vascular structures, in a total of 37 patients, after surgery infiltration was detected in a total of 15 patients, and in 22 patients contact was without infiltration. At 2 (5.4%) cases, we had false positive findings.
and hilar lymph nodes on the basis of the estimated stage of the disease. According to CT findings of thoracic organs in our subjects, we determine the stages of the disease on the basis of TNM classification. CT results are compared with post-operative, and calculated are the accuracy, sensitivity and specificity of imaging methods, as well as PPV and NPV values.

Among our respondents there were significantly more men than women (6.5:1), which differs somewhat from the data from the literature of the world where the ratio is lower in some countries and almost equal (Scotland, United Kingdom) where the bronchus cancer in the last decade became the most lethal cancer in women (21%).

Most frequent age group in men was between 50-69 years and, among women 50-59. It is believed that the disease incidence and morbidity show a further increase in smokers in particular both women and men.

Out of 60 patients with malignant neoplasm of the lungs pathohistological representation was as follows: the most common type was squamous cell tumors 49 (81.6%), and adenocarcinoma in 9 (15%), while bronchoalveolar and macro cellular types were rare, 1.7%. Squamous cell cancer in men at older age group of 50-69 years was represented in 33% and adenocarcinoma in women was more pronounced (44.4%) in younger age from 40 to 49 years. The literature states that the most common lung cancer in smokers is of planocellular type and non-smokers adenocarcinoma, especially in women of younger ages corresponding to our own results.

In the analysis of T stage disease tumor contact with macro vascular mediastinal structures was recorded in 37 (61.6%) cases, with chest wall in 14 (23.3%), while the T stage in the form of existence solitary lung lesions is recorded in 9 patients. Analysis of CT findings in our subjects established dominance of stage T2 disease (40%), whereas T1 and T4 were equally represented (26.67%). T3 stage was found only at 11.67% of cases.

Postoperatively all patients was analyzed and the validity of CT findings was found as 40 positive, 13 truly negative, 4 false positive and 3 false negative findings. This is determined the following values of statistical parameters of CT methods: sensitivity of 93%, specificity 76.40, the accuracy of 83.33%, a PPV of 90.9 and NPV of 81.29%.

Evaluation of lymph nodes done changes in size is found in 21 of 49 patients (4 patients with T-1 and 17 with T-2 lesions). Most of them belong to N0 stage (46.6%), stage N1 is determined in 23.33, 26.66% in N2 and N3 in 3.33% cases. Mediastinal tumor nodes in the upper right paratracheal region (labeled 2R Node mapping scheme according to American Thoracic Society) were found in one patient; nodes in the right lower paratracheal region (4R) in 8 patients, the right trachea bronchial region (10R) at 4, sub cortically (location 7) in 7 and aortopulmonary (location 5) in one case. After the surgery results are compared and there was 5% false positive (reactive lymphadenopathy) and 13.33% false negative (metastases in nodes size <1cm) on CT findings. They have affected the level of the value of statistical parameters: sensitivity of 90.00%, specificity 64%, accuracy 86.67, PPV 67, NPV 89.28%.

Prevalence of mediastinal metastases of 43% agrees with the data of some surgical research done on large samples (14, 15), which supports our conclusion regarding the value of CT in mediastinal staging of disease. In most previous studies lacked precise radiological-surgical correlation, so that high precision for any given group of nodes could not be achieved. Numerous papers in the scientific literature have evaluated the
value of CT in staging of non-small cell lung cancer which has not yet reached full consensus on the value of the relevant statistical parameters. Our results are similar to those of Herman et al., and Barton et al. (7, 16) that highlight the high sensitivity and poor specificity of CT in assessing mediastinal adenopathy in patients with lung cancer.

Our results and experiences and results from similar research, strongly suggest that CT plays an important role in preoperative staging accuracy in patients with lung cancer and contribution to the determination of adequate therapy. Negative CT findings according to our experience and other authors are highly valid in the exclusion of mediastinal metastasis, which is practically reducing the need for surgery. Positive CT findings are less reliable, and should not be decisive in assessing the operability. Positive CT findings of increased detection and localization facilitate biopsy of the nodes before curative resection. We agree that there is no strict size of lymph nodes which would be a reliable criterion in lung cancer staging due to microscopic metastases in lymph nodes of normal size and increase in cases of reactive hyperplasia, mediastinal lipomatosis and dystopic mediastinal thyroid. (13).

We believe that it is not possible to give a final evaluation of the definite role of CT in lung cancer staging despite to the constant improvement of diagnostic equipment, although we found its value and the performance in our study certainly convinced. “Staging System” is now generally accepted clinical methodology that helps in quality clinical approach to lung cancer and reducing number of exploration thoracotomy, although even it does not cover all possible variants of disease. In the near future we expect new molecular predictors prognosis and taking more diagnostic parameters for determining the degree of tumor extension, “International Staging System” with the help of CT and then to remain the best guide to setting up prognosis.

6. CONCLUSIONS

- CT proves to be a quality diagnostic method for evaluation of lymph node invasion with sensitivity of 90%, specificity 83.3%, and accuracy 86.67%, PPV 84.37% and NPV 89.28%.
- CT accuracy in evaluation of operable cases in patients with I, IIa and IV was 100%, IIIb stage (87%), while the lowest (70%) was in case of patients with stage IIIa, which is often a diagnostic dilemma – to differentiate IIIa from IIIb stage.
- Research results indicates that the overall sensitivity of CT in evaluation of lung cancer based on TNM classification is 76.4%, specificity 93.0%, accuracy 88.333%, PPV 99.90% and NPV 81.25%
- Based on this we can conclude that CT is indispensable diagnostic method in evaluation of tumor operability.

REFERENCES


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