Pre and post operative diagnosis of lung cancer patients: Is there a concordance?

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KEYWORDS
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Abstract  Background: The diagnosis of lung cancer is essential to customize the care of patients. Their management is based on histological diagnosis and extent of disease at time of diagnosis.

Aim of the study: To study the impact of preoperative and postoperative pathological diagnosis of a group of patients managed for lung cancer.

Patients and methods: This study was a single-center retrospective study. The duration of inclusion was 4 years (1 January 2011–31 December 2014). We compared the preoperative pathological outcomes of medical procedures and postoperative histological data. Data values were estimated in percentage.

Results: One hundred patients were included in the study. The concordance rate between preoperative and postoperative diagnoses across all histological types, was 68%. The misdiagnosis rate and incomplete diagnosis rates were 10% and 22%. There were discrepancies regardless of diagnostic histologic type. Concordance rates of endoscopy, the trans-bronchial puncture, echo-endoscopy, and CT-puncture were 74%, 77%, 46%, and 66% respectively.

Conclusion: Our study shows pre and postoperative discrepancy in nearly 30% of cases. This finding should be taken into account because it can change the therapeutic management of these patients in particular of non-operated patients.

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Introduction

The management of lung cancer is based on histological diagnosis and extent of disease at diagnosis, determined by the TNM [1] classification. Currently, Lung cancer is the most common cancer worldwide, accounting for 1.61 million new cases annually representing 12.7% of all new cancers. It is also the most common cause of death from cancer, with 1.38 million deaths (18.2% of the total). The majority of the cases now occur in the developing countries (55%) [2]. Lung cancer is ranked fifth among male population and thirteenth among female population. It affected (73.6%) males and (26.4%) females with a male to female ratio of 279:100 [3]. Three quarters of patients with non-small cell lung cancer are diagnosed with locally advanced (stage IIIIB) or metastatic (stage IV),
unresectable [3]. Chemotherapy for these patients is the primary therapeutic option. The choice of a different protocol of chemotherapy regimens is guided largely by histological typing and immunohistochemical profile of the tumor so the treatment is specific for each cell type: small cell carcinoma, squamous cell carcinoma and adenocarcinoma. During the last decade, researches, including genetic, have enabled the development of targeted therapies. Patients with adenocarcinoma can currently benefit from specific treatments based on tumor mutations. The individualization of these biomarkers has amended decision algorithms therapist. Having a reliable diagnosis has become essential to customize the care of patients. The vast majority of lung cancer diagnoses is obtained from small biopsies performed during non-surgical procedures. The small size of samples and the small amount of tissue obtained from these methods can make it difficult or impossible for the achievement of all pathological examinations. The reliability of the diagnosis can then be questioned.

Patients and methods

This study was a single-center retrospective study. The duration of inclusion was 4 years (1 January 2011–31 December 2014). In total, 200 patients were followed up in our hospital for lung cancer. 150 had had a surgery for diagnostic or therapeutic purposes at cardiothoracic department Zagazig university hospital. Of these, 100 who had a preoperative diagnosis were included in this study.

The objective of this study was to verify the correlation between the preoperative and postoperative histological diagnosis. A preoperative diagnosis of lung carcinoma formal had to be obtained by medical method (bronchoscopy, Trans-bronchial aspiration (TBNA), Sputum cytology and Computed tomography (CT) C-T guided biopsy). The final diagnosis was obtained only through surgical method (wedge resection, pleural biopsies, segmentectomy, lobectomy, pneumonectomy, lymph node biopsies). Each patient had a complete sheet, including: a physical examination, chest radiography (anteroposterior and lateral), a chest CT, abdominal and brain, and fiber optic Rigid bronchoscopy. The operability sheet included: ECG, pulmonary function tests, a gas analysis, and laboratory tests. Where necessary, more complex explorations complete the assessment: cardiac ultrasound, cardiac and cardiopulmonary effort test, myocardial perfusion and ventilation/perfusion scan. For each patient we studied preoperative histological type, preoperative diagnostic method, postoperative histology, and postoperative diagnostic method. We excluded patients with preoperative diagnosis other than lung cancer and patients with no preoperative diagnosis. According to this we divide the patients into:

Group 1-concordant diagnosis: pre and postoperative histology is identical. Group 2-misdiagnosis: unconfirmed final diagnosis of cancer or different pre- and postoperative histological types. Group 3-incomplete diagnosis: a final diagnosis of tumor is of composite histology or undifferentiated tumor, to be specified by surgery. The results of the matches were expressed as a percentage.

Results

Table 1: Diagnostic methods. One hundred patients were included in the study. The average age was 62 years. 75 were male (75%) and 25 were women (25%). Preoperative diagnoses were obtained by 61 fiber optic bronchoscopes, 14 TBNA, 6 sputum cytology, 19 Computed tomography (CT) guided biopsy.

Table 2: Surgical techniques used for diagnosis. Postoperative diagnoses were obtained by lobectomy in 56 patients (56%), pneumonectomy 17, 1 pleuropneumonectomy total of 18 patients (18%), 8 segmentectomy and atypical resections (8%), 4 pleural biopsies (4%), 14 video mediastinoscopy and mediastinal exploration (14%).

Table 3 Group of patients and concordance. Patients were classified into 3 groups: (concordant Group 1): The preoperative histology is corresponding to the definitive diagnosis in 68 patients (68%). (Group 2): The preoperative misdiagnosis is presented in ten patients (10%). (Group 3): The preoperative diagnosis was incomplete in 22 patients (22%).

Table 4 and Fig. 1 Pre-and post-operative diagnostic pathology. The preoperative histology is corresponding to the definitive diagnosis (concordant Group 1) in 68 patients (68%): 29 patients adenocarcinoma (42.6%); 30 patients squamous cell carcinomas (44.1%); 4 carcinoid tumors (2 typical and 2 atypical) (6%); 2 small cell carcinomas (SCC) (2.9%); 2 non-small cell carcinomas (NSCC) (2.9%) and 1 case of sar-
coma (1.5%). The preoperative misdiagnosis (Group 2) is presented in ten patients (10%): 4 patients had different pre and postoperative diagnoses (4%); 6 patients (6%) had a diagnosis of fibro elastic scar with no residual tumor found in the surgical specimen. The preoperative diagnosis was incomplete (Group 3) in 22 patients (22%). 12 patients (12%) had final diagnosis of composite tumor, having at least two histological subtypes. For 10 patients (10%) with an initial diagnosis of undifferentiated carcinoma, surgery could specify the histological type. Concordance rate of pre and postoperative diagnoses varies depending on the histological type: The preoperative diagnosis of histological type of adenocarcinoma is presented in 38 patients, 29 patients of them have confirmed diagnosis by surgery (76%), 6 patients (16%) (4 tumors consider it to its lipid component, 1 has a neuroendocrine large cell component, and 1 has a sarcomatoid component), 3 patients (8%) had misdiagnosis. 3 adenocarcinomas were ultimately different histological lesions (1 patient had sarcomatoid carcinoma, 1 patient had a large cell carcinoma and 1 patient had small cell carcinomas). The preoperative diagnosis of histological type of squamous cell carcinoma is presented in 37 patients, 30 patients of them have confirmed diagnosis by surgery (81%). 2 patients with squamous cell carcinoma had a composite tumor (5%) (In one patient is linked to basal cell adenocarcinoma and in the other 1 patient is linked to small cell carcinoma), 5 patients were misdiagnosed (14%) in 2 patients, the diagnosis was different (2 patients with squamous cell carcinoma had finally adenocarcinoma, non-small cell lung cancer) and the other 3 patients had fibro elastic scar.

The preoperative diagnosis of histological type of carcinoma tumor, was confirmed in 100% of cases. We have 4 patients (2 typical and 2 atypical).

Three patients had a preoperative diagnosis of small cell carcinoma and the diagnosis was confirmed on 2 separate sessions, a concordance rate of 67%. In one case (33%), the final tumor histology was a composite tumor combining component of a small cell carcinoma and adenocarcinoma component.

Two patients had a preoperative diagnosis of sarcomatoid tumor. The diagnosis was confirmed in 50% of cases. 1 patient had a preoperative diagnosis of large cell carcinoma. The final diagnosis was an adenocarcinoma (concordance rate of 0%).

The preoperative diagnosis of histological type of non-small cell carcinoma, was presented in 16 patients, 7 of non-small cell carcinoma patients (43.6%) had adenocarcinoma, 2 patients (12.5%) had squamous cell carcinoma, 1 patient (6.3%) had small cell carcinoma, 1 patient (6.3%) had large cell carcinoma, two patients (12.5%) had composite tumor, 2 patients (12.5%) had fibro elastic scar and in one patient (6.3%), it could not be specified by surgery.

Tables 5 and 6 and Figs. 2 and 3: The pre and postoperative histological concordance rates also vary depending on the diagnostic methods. Among the 101 patients who underwent endoscopy, preoperative diagnosis was obtained by this method in 61 patients (60.4%). The pre and postoperative histology were identical in 45 cases, with a concordance rate of 74%. The sensitivity of bronchoscopy was 45%. The cancer diagnosis was wrong in 10 patients (9.9%): 7 patients (7%) had different diagnoses and 3 patients (3%) had a fibro elastic scar.

In 30 cases (29.7%), the preoperative diagnosis was incomplete: 15 patients had a histological result of composite tumor (15%) and 15 other had preoperative diagnosis of non-small cell lung cancer (surgery has helped to specify the diagnosis).

Eighteen patients underwent a TBNA. Fourteen Preoperative diagnoses were obtained by this method (78%). In 10 patients (71% concordant rate), the final histological findings corresponded to preoperative diagnoses. The sensitivity of TBNA was 55.5%. In 2 cases the diagnosis was wrong. In other 2 patients, the diagnosis is unclear.

Table 4: Pre-and post-operative diagnostic pathology.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Total No.</th>
<th>Adenocarcinoma</th>
<th>Sq.cell.CA</th>
<th>Carcinoid</th>
<th>Small cell CA</th>
<th>Sarcoma</th>
<th>N.S.C.CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
<td>38</td>
<td>37</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Post.Op.other path.</td>
<td>9–24%</td>
<td>7–19%</td>
<td>4–100%</td>
<td>2–67%</td>
<td>0–0%</td>
<td>6–37.5%</td>
<td></td>
</tr>
<tr>
<td>Post. Op. Confirmed path.</td>
<td>29–67%</td>
<td>30–81%</td>
<td>4–100%</td>
<td>1–33%</td>
<td>1–50%</td>
<td>10–62.5%</td>
<td></td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Non-surgical Methods of diagnosis</th>
<th>Fiber optic endoscope</th>
<th>TBNA</th>
<th>Sputum cytology</th>
<th>C-T guided biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of Pts.</td>
<td>101</td>
<td>18</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>No. of Pre.op. diagnosis</td>
<td>61</td>
<td>14</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Identical path.pre.Post.op.</td>
<td>45</td>
<td>10</td>
<td>2</td>
<td>13</td>
</tr>
</tbody>
</table>
Thus, the heterogeneity of primary lung carcinoma [5,6]. Thus, they have many histological types and subtypes, illustrating the evolution and become more complex, taking into account the histological classification of lung cancer has been demonstrated in patients with EGFR expression as negative. The search for EGFR mutations can be performed on any biological sample containing tumor cells, and profitability will depend on the abundance of tumor cells, the amount of material available, the representativeness of the molecular abnormality described as well as the technique used. To do this research on small biopsy material, a cytological sampling and on a surgical specimen. However, as regards the first two types of samples, material management by the pathologist is essential to enable the achievement of the different techniques that qualify the tumor material [15]. Having a reliable histological diagnosis has become paramount or more important than anything else but most of them are obtained by non-surgical methods, which may have consequences in terms of reliability [16]. Finally, within our multidisciplinary consultation meetings, it is not uncommon to find a discrepancy between the preoperative diagnosis and postoperative diagnosis. These reasons motivated us to perform this study, especially since few studies have verified the consistency of pre and postoperative diagnoses and most are interested only distinguish between small cell carcinoma and non-small cell carcinoma [17].

Concordance rate between pre and postoperative histological types in our study is 68%. In almost one third of cases, the preoperative diagnosis is either wrong or incomplete. This high discrepancy shows that having a reliable diagnosis is not obvious. In case of doubt about the quality of the examination done, the creation of new biopsies should be done.

In our study, non-surgical methods explorers have not made the diagnosis in 16% cases (adenocarcinoma). These patients without diagnosis from surgical biopsies, have not benefited from adequate adjuvant treatment and the biomarkers tests would not have been realized. These non-diagnostic results therefore have important therapeutic implications. These errors also apply to other histological types. These errors also apply to other histological types.

Discussion

Over time, the histological classification of lung cancer has evolved and become more complex, taking into account the histological data, immunohistochemical and genetic. There are four major forms of lung cancer (squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma) described by Kreyberg in 1967 [4], we currently have many histological types and subtypes, illustrating the heterogeneity of primary lung carcinoma [5,6]. Thus, the survivals are different depending on the type and histologic subtype: Yim et al. [7] as well as other studies [8,9] showed that patients with a lipid adenocarcinoma or having a lipid component have a significantly higher survival of patients with invasive type of adenocarcinoma. Kawase et al. studies [10] and Asamura et al. [11] showed significant differences in survival according to histology (adenocarcinoma and squamous cell carcinoma). The chemotherapy protocols also differ according to histological type: Scagliotti et al. [12] concluded that cisplatin-pemetrexed combination brings a benefit in terms of survival for patients with adenocarcinoma. Similarly, molecular biology has enabled the development of targeted therapies to individualize patient treatment. Studies have shown that patients with adenocarcinoma and EGFR mutation carriers have a gain in survival when treated with targeted therapies [13,14]. In addition, no benefit in terms of survival or other clinically relevant effects of tyrosine kinase inhibitor therapy has been demonstrated in patients with EGFR expression as negative. The search for EGFR mutations can be performed on any biological sample containing tumor cells, and profitability will depend on the abundance of tumor cells, the amount of material available, the representativeness of the molecular abnormality described as well as the technique used. To do this research on small biopsy material, a cytological sampling and on a surgical specimen. However, as regards the first two types of samples, material management by the pathologist is essential to enable the achievement of the different techniques that qualify the tumor material [15]. Having a reliable histological diagnosis has become paramount or more important than anything else but most of them are obtained by non-surgical methods, which may have consequences in terms of reliability [16]. Finally, within our multidisciplinary consultation meetings, it is not uncommon to find a discrepancy between the preoperative diagnosis and postoperative diagnosis. These reasons motivated us to perform this study, especially since few studies have verified the consistency of pre and postoperative diagnoses and most are interested only distinguish between small cell carcinoma and non-small cell carcinoma [17].

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Their consequences are not insignificant since the beginning of research to explore the interest of biomarker research of mutations, including squamous cell carcinoma [13]. Several hypotheses can be advanced to explain this discrepancy: Due...
to the heterogeneity of adenocarcinomas and lung cancer in general [18], the small biopsies may not be representative of the tumor as a whole. The main difficulty in the classification of poorly differentiated tumors, differentiated component which is difficult or impossible to appreciate given the small size of samples. The second difficulty concerns the so-called composite or mixed tumors.

In our trial, they represent 10% of the lesions. The main problem is the almost exclusive presence of a determinant quantity of tumor at a biopsy [19]. The small amount of tumor tissue obtained from non-surgical procedures can make it difficult or impossible the achievement of all histological analyzes, immunological and genetic due to the “exhaustion” of the blocks.

Currently, there are no prospective data assessing the amount of tumor tissue obtained according to the used sampling techniques. The amount of tissue also influences the quality of examinations performed. Moreover, in a study comparing the expression of biomarkers based on the type of sample technique (bronchial biopsy versus surgical specimen) in patients with adenocarcinoma, Cutter et al. [20] show a discrepancy in EGFR expression significantly.

Our study has several limitations: it is a retrospective trial, single-center whose small population limits the power of the study. However, other trials with more staff and made in several centers could help confirm or not our results.

Conclusion

The message of our study is not to say that surgery should be the only diagnostic tool in the management of lung cancer. However, account must be taken of the discrepancy between the preoperative diagnosis and postoperative diagnosis observed in our trial to be able to propose if necessary the creation of new biopsies to clarify a diagnosis or to check for biomarkers in order to adapt a therapeutic protocol. If in the near future, the development of techniques allow a refinement of diagnosis from a smaller amount of tumor tissue, we must now focus on methods to achieve maximum material and with minimum risk to patients.

Conflict of Interest

There is no conflict of interest.

References