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Original Research Article.

Analysis of Prognostic and Predictive Value of the Newly Proposed Grading System of Invasive Pulmonary Adenocarcinoma: An Institutional Based Study

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ABSTRACT

Objective: The aim of the present study is to analyze the prognostic and predictive value of the newly proposed grading system of invasive pulmonary adenocarcinoma.

Materials and Methods: The present study included 200 patients with pulmonary adenocarcinoma for the study. The diagnosis of LY was based on the immunostaining results for D2-40 to validate the location of the lymphatic duct. To determine the degree of tumor invasion above the elastic layer of the vessels and the visceral pleura, the presence of PL and V is evaluated by means of elastic van Gieson staining.

Result: The stage 0 recorded predominantly in lepidic, acinar, papillary, and micropapillary histologic patterns (75% of the cases), whereas only 25% were recorded in solid and complex glandular patterns. Likewise, high-grade cytology was seen predominantly in solid and complex glandular patterns (60% of the cases), whereas it was recorded in 30% of acinar, papillary, and micropapillary patterns, and 5% in lepidic pattern.

Conclusion: The 2011 IASLC/ATS/ERS adenocarcinoma classification can have an impact on TNM staging. It may help in comparing histologic characteristics of multiple lung adenocarcinomas to determine whether they are intrapulmonary metastases versus separate primaries. it may be more meaningful clinically to measure tumor size in lung adenocarcinomas that have a lepidic component by using invasive size rather than total size to determine the size T factor.

Keywords: Adenocarcinoma; Tumor Grading; Lung, Prognosis.

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INTRODUCTION

Lung cancer is the most frequent cause of major cancer incidence and mortality worldwide.[1,2] Adenocarcinoma is the most common histologic subtype of lung cancer in most countries, accounting for almost half of all lung cancers.[3] A widely divergent clinical, radiologic, molecular, and pathologic spectrum exists within lung adenocarcinoma. As enormous resources are being spent on trials involving molecular and therapeutic aspects of adenocarcinoma of the lung, the development of standardized criteria is of great importance and should help advance the field, increasing the impact of research, and improving patient care. This classification is needed to assist in determining patient therapy and predicting outcome. The 2015 WHO classification of pulmonary adenocarcinoma,[4] based on the predominant histologic pattern, has consistently been found to correlate with prognosis and separates adenocarcinoma into the three following prognostic groups: low grade (lepidic predominant); intermediate grade (acinar or papillary predominant); and high grade (solid or micropapillary predominant). There are also suggestions that the classification and stratification by the predominant pattern is predictive of response to adjuvant chemotherapy.[5]

The aim of the present study is to analyze the prognostic and predictive value of the newly proposed grading system of invasive pulmonary adenocarcinoma.

MATERIALS AND METHODS

We identified 300 patients who underwent resection of a dominant, primary, pulmonary adenocarcinoma. A lesion was defined as dominant if it was one of the following: (1) positive on positron emission tomography (standardized uptake value > 2.5) and/or negative on positron emission tomography but was

enlarged in total size and/or size of the solid component; or (2) was clinically suspicious for malignancy, as assessed by a thoracic surgeon. After careful review of all patients, the following patients were excluded: 1 who did not have pathology slides available for re-evaluation; who had clinical N2 disease and had received induction chemoradiation therapy; who had advanced disease at presentation; who had mucinous adenocarcinoma subtype; who had multiple synchronous primary tumors; and who had stage II or III disease.

Thus, 200 patients who had pulmonary adenocarcinoma were included in the study. Adenocarcinoma in situ, minimally invasive adenocarcinomas, multifocal adenocarcinomas, invasive mucinous adenocarcinoma, and other variants of adenocarcinoma were excluded from the study.

Pathologic Diagnosis and Grading Criteria

Pathologic staging was determined according to the eighth edition of the TNM classification of malignant tumors.[6] All patients underwent pathologic examination using the WHO classification.[7] The current pathologic grading was based on the predominant subtype, which are as follows: grade 1, lepidic predominant; grade 2, acinar or papillary predominant; and grade 3, solid or micropapillary predominant.[5] The proposed pathologic grading was based on the following grading criteria, which was recently proposed by the IASLC: grade 1, lepidic predominant tumor, with less than 20A–E.% of high-grade patterns; grade 2, acinar or papillary predominant tumor, with less than 20% of high-grade patterns; and grade 3, any tumor with greater than or equal to 20% of high-grade patterns (solid, micropapillary, and/or complex gland). All patients were evaluated for lymphatic invasion (LY), vascular invasion (V), and pleural invasion (PL). The diagnosis of LY was based on the immunostaining results for D2-40 to validate the location of the lymphatic duct. To determine the degree of tumor invasion above the elastic layer of the vessels and the visceral pleura, the presence of PL and V is evaluated by means of elastic van Gieson staining.

Statistical Analysis

Categorical variables were summarized using counts and percentages, whereas continuous variables were summarized using median values and interquartile ranges. Data between groups were compared using an independent t test for continuous data, as well as c2 analysis for categorical data. Cancer-specific survival probability was calculated using the Kaplan-Meier method, with 95% confidence intervals (CIs), and differences in survival were evaluated using the log-rank test. Five-year disease-free survival (DFS) and overall survival were calculated from the date of surgical intervention until the date of recurrence or cancer-related death, respectively. All statistical analyses were performed using SPSS, version 19.0 (SPSS Inc, Chicago, Ill).

Table 1: Patients' demographic Information

	Stage 0 (n=100)	Stage 1 (n=100)
Age	69.2 ± 8.9	69 ± 9.2
Sex		
Male	60	30
Female	40	70
History of lung cancer	5	7
Smoking history	40	30
Clinical stage		
IA	65	60
IIA	30	35
IIIA	05	5

Table 2: Patient's characteristics

Characteristics	Stage 0 (n=100)	Stage 1 (n=100)	P value
Type of surgery			0.050
Lobectomy	40	35	
Segmentectomy	30	35	
Wedge resection	20	20	
Pneumonectomy	10	15	
Invasive characteristics			<0.001
LY	30	35	<0.001
V	40	45	<0.001
PL	30	20	<0.001
Pathologic stage			<0.002
IA	60	70	
IB	40	30	
IIA	0	0	
IIB	0	0	
IIIA	0	0	
IIIB	0	0	
Predominant histologic pattern			<0.001
Acinar	30	15	
Papillary	25	10	
Lepidic	10	5	
Solid	20	35	
Micropapillary	10	5	
Complex glands (cribriform and fused glands)	5	25	

RESULTS

The characteristics of the patients are illustrated in table 2. The stage 0 recorded predominantly in lepidic, acinar, papillary, and micropapillary histologic patterns (75% of the cases), whereas only 25% were recorded in solid and complex glandular patterns. Likewise, high-grade cytology was seen predominantly in solid and complex glandular patterns (60% of the cases), whereas it was recorded in 30% of acinar, papillary, and micropapillary patterns, and 5% in lepidic pattern.

DISCUSSION

The result shows the efficacy of the new criteria. In our study, the prognosis of patients with pathologic stage 0 or I was well stratified by this grading but not in patients with pathologic stage II or III. The prognosis of completely resected stage I NSCLC is expected to be favorable. However, several patients experience recurrence after complete resection, such that the 5-year disease-free survival rates for clinical stage IA and stage IB disease are 84.3% and 65.8%, respectively.[8] The aim of the present study is to analyze the prognostic and predictive value of the newly proposed grading system of invasive pulmonary adenocarcinoma.

Although the rationale for integration of the 2 staging systems is multifaceted, the clinical utility lies in allowing accurate assignment to an anatomic and pathologic stage that is strongly associated with patient outcomes and prognosis and can thus inform further management and counseling. The results reveal that a grading system based on a histologic pattern is a strong prognostic classifier of invasive pulmonary adenocarcinoma. Given that it builds directly from the current classification system, it can be readily and reproducibly applied in practice. The proposed IASLC grading system considers the heterogeneity and relative proportion of architectural patterns within a tumor to arrive at a common language for prognostic groups, thus, paving the way for studies evaluating response and prognosis of pulmonary adenocarcinoma.

Some investigators have proposed a molecular grading system on the basis of cell cycle gene expressions as a way to predict recurrence in stage I to II tumors36-38; however, no reference to a histologic evaluation is available in these studies. It is hoped that future studies may be able to incorporate the IASLC grading system in their investigations to identify other biomarkers that can improve prediction of recurrence of the disease or death. Lepidic growth may be composed of neoplastic cells with nuclear atypia resembling that of the adjacent invasive tumor. Some observers would further argue that such lepidic patterns correspond to an aerogenous spread of tumor cells but are no longer an “in situ” component.[9]

Many reports have concluded that the pathologic invasive component size, as opposed to the total tumor size, is associated more significantly with malignant behavior and prognosis; and they have confirmed that when the invasive component of a lesion is>5 mm, rates of recurrence rise and survival decreases significantly.[7,10-13] Use of comprehensive histologic subtyping along with other histologic characteristics has been shown to behavior.[14]

CONCLUSION

The 2011 IASLC/ATS/ERS adenocarcinoma classification can have an impact on TNM staging. It may help in comparing histologic characteristics of multiple lung adenocarcinomas to determine whether they are intrapulmonary metastases versus separate primaries. It may be more meaningful clinically to measure tumor size in lung adenocarcinomas that have a lepidic component by using invasive size rather than total size to determine the size T factor. The novel grading system not only demonstrated prognostic significance in stage I IPA but also offered clinical value for directing therapeutic decisions regarding adjuvant chemotherapy.

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