

Impact of Histologic Subtyping on Outcome in Lobar vs Sublobar Resections for Lung Cancer

A Pilot Study

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OBJECTIVE: The 2011 International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) classification of pulmonary adenocarcinomas introduces adenocarcinoma in situ and minimally invasive carcinoma and categorizes adenocarcinoma with more extensive invasion by the predominant subtype. Data have shown that wedge or segmentectomy (W/S) may be appropriate for in situ and minimally invasive adenocarcinoma, but whether sublobar resection is appropriate for tumors with more extensive invasion is unclear. The aim of this pilot study is to evaluate whether there are any trends regarding the impact of invasion and subtypes of carcinoma regarding survival in lobectomy vs W/S procedures using a comprehensive histologic evaluation.

METHODS: Eighty-five surgical specimens (59 lobectomies, 26 W/Ss) were reviewed. Histologic type, size, pleural, lymphovascular invasion, and necrosis were recorded. Adenocarcinomas were classified by 2011 IASLC/ATS/ERS guidelines with each histologic pattern recorded as a percentage of the total tumor. Statistical analysis was performed using SAS, version 9.2. Proportional hazards regression analysis was used to evaluate survival according to resection type (lobectomy or W/S) adjusting for tumor size and the predominant histology.

RESULTS: Multivariate analysis did not show a statistically significant difference in survival between lobectomy and W/S specimens adjusting for tumor size, regardless of histologic subtype or other negative predictors of prognosis ($P = .7704$).

CONCLUSIONS: Our findings corroborate the prognostic significance of the 2011 adenocarcinoma subtyping classification and additionally suggest that lobectomy does not offer an overall survival advantage over W/S regardless of histologic subtype. Therefore, this finding suggests that limited resection may be appropriate for small size tumors, particularly those ≤ 2 cm with invasive histology.

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ABBREVIATIONS: ADC = adenocarcinoma; AIS = adenocarcinoma in situ; ATS = American Thoracic Society; BAC = bronchioloalveolar carcinoma; ERS = European Respiratory Society; IASLC = International Association for the Study of Lung Cancer; MIA = minimally invasive adenocarcinoma; NSCLC = non-small cell lung carcinoma; VPI = visceral pleural invasion; WHO = World Health Organization; W/S = wedge or segmentectomy

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The surgical management of non-small cell lung carcinoma (NSCLC) has been an issue of debate since the early 1970s when anatomic segmentectomy was proposed as a possible treatment of stage I NSCLC.¹ With the advent of more advanced radiographic techniques, the detection of small lesions and ground-glass opacities has increased,² and the issue of whether to perform a lobectomy or a lesser surgical procedure, that is, segmentectomy or wedge resection, has met with renewed interest and remains controversial.³⁻⁵ The focus on radiographic ground glass opacities and small peripheral lesions, which largely correspond to adenocarcinomas (ADCs), prompted an intense study of this particular carcinoma subtype over the past two decades.⁶⁻⁹ The culmination of this review resulted in an updated classification of ADC issued by the International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS), which was published in 2011 (Table 1).¹⁰ In addition to other guideline revisions from previous classification systems,¹¹ this revision introduced the concepts of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA). These two categories of ADC are associated with virtually 100% 5-year survival and, evidence suggests, are potentially amenable to treatment with either wedge or segmentectomy (W/S).^{10,12-14} However, AIS and MIA account for only a small percentage of all lung carcinomas,¹⁰ with the vast majority of non-small cell carcinomas having a much poorer prognosis even at stage I.¹⁰ While the updated ADC classification scheme has been shown to correlate with prognosis, the impact of histologic subtype based on the updated classification system has not been thoroughly evaluated in regard to overall survival based on type of resection. The aim of this pilot study is to eval-

TABLE 1] 2011 IASLC/ATS/ERS Classification of Pulmonary ADCs¹⁰

Classification
Preinvasive lesions
Atypical adenomatous hyperplasia
AIS (≤ 3 cm formerly BAC)
Nonmucinous
Mucinous
Mixed mucinous/nonmucinous
MIA (≤ 3 cm lepidic predominant tumor with ≤ 5 mm invasion)
Nonmucinous
Mucinous
Mixed mucinous/nonmucinous
Invasive ADC
Lepidic predominant (formerly nonmucinous BAC pattern, with > 5 mm invasion)
Acinar predominant
Papillary predominant
Micropapillary predominant
Solid predominant with mucin production
Variants of invasive ADC
Invasive mucinous ADC (formerly mucinous BAC)
Colloid
Fetal (low and high grade)
Enteric

ADC = adenocarcinoma; AIS = adenocarcinoma in situ; ATS = American Thoracic Society; BAC = bronchioloalveolar carcinoma; ERS = European Respiratory Society; IASLC = International Association for the Study of Lung Cancer; MIA = minimally invasive adenocarcinoma.

uate the potential significance of histologic subtype regarding survival in lobectomy vs W/S procedures, incorporating a comprehensive histologic approach.

Materials and Methods

A retrospective review of 85 surgical specimens from patients with NSCLC (59 lobectomy specimens, 19 wedge resections, and seven segmentectomy specimens) from the Department of Thoracic Surgery of The Mount Sinai Hospital obtained during the period of 2002 to 2010 were reviewed. Only node-negative tumors and resections with negative margins were included in order for the dataset to be as uniform as possible. The rationale in limiting our pilot study to patients that had node-negative results was to focus on the impact of histology and minimize confounding factors. Histologic type, tumor size, and the presence of pleural, vascular, or lymphatic invasion and necrosis were recorded. Subtypes of ADC were classified according to the 2011 IASLC/ATS/ERS guidelines with each histologic pattern recorded as a percentage of the total tumor. Non-ADC tumors were classified by current World Health Organization (WHO) criteria. All histologic sections were reviewed by two pathologists, with cases of ADC reclassified using 2011 guidelines as necessary. As there is currently no accepted grading system for lung carcinomas, grade was not separately evaluated. Tumors ≤ 3 cm were

submitted entirely for histologic evaluation, and tumors > 3 cm were submitted at a minimum of one section per centimeter of tumor to ensure accurate classification of ADC in particular. Tumor size was taken from the pathology reports and verified with the findings on the histologic slides. For purposes of this study, the overall tumor size was used in the analysis to align with current American Joint Committee on Cancer (AJCC) staging guidelines. Comparison was made between patients with sublobar resections (W/S) vs patients who underwent lobectomy. Data including patient demographics, pathologic staging, and post-operative follow-up were obtained from surgical pathology reports and patients' medical records. Pathologic staging was performed in accordance with the seventh edition of guidelines established by the AJCC.¹⁵ Mount Sinai Institutional Review Board approval was obtained and individual consent for the study waived (Mount Sinai IRB IF1322786).

Statistical Analysis

Statistical analysis was performed using SAS, version 9.2 (SAS Institute Inc). Proportional hazards regression analysis was used to determine whether survival differed according to resection type (lobectomy or

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