Radiologic Evaluation of Small Lepidic Adenocarcinomas to Guide Decision Making in Surgical Resection

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Background. **The International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society classification of pulmonary adenocarcinomas identifies indolent lesions associated with low recurrence, superior survival, and the potential for sublobar resection. The distinction, however, is determined on the pathologic evaluation, limiting preoperative surgical planning. We sought to determine whether preoperative computed tomography (CT) characteristics could guide decisions about the extent of the pulmonary resection.**

Methods. **We reviewed the preoperative CT scans for 136 patients identified to have adenocarcinomas with lepidic features on the final pathologic evaluation. The solid component on CT was substituted for the invasive component, and patients were radiologically classified as adenocarcinoma in situ, 3 cm or less with no solid component; minimally invasive adenocarcinoma, 3 cm or less with a solid component of 5 mm or less; or invasive adenocarcinoma, exceeding 3 cm or solid component exceeding 5 mm, or both. Analysis of variance, *t* test, χ^2 test, and Kaplan-Meier methods were used for analysis.**

Results. **The radiologic classification identified 35 adenocarcinomas in situ (26%) and 12 minimally invasive (9%) and 89 invasive adenocarcinoma (65%) lesions. At a 32-month median follow-up, patient outcomes associated with the radiologic classification were similar to the pathologic-based classification: the radiologic classification identified 14 of 16 patients with recurrent disease and all 6 who died of lung cancer. In addition, patients with radiologic adenocarcinoma in situ and minimally invasive adenocarcinoma who underwent sublobar resections had no recurrence and 100% disease-free and overall survival at 5 years.**

Conclusions. **The radiologic classification of patients with lepidic adenocarcinomas is associated with similar oncologic and survival outcomes compared with the pathologic classification and may guide decision making in the approach to surgical resection.**

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Current radiographic techniques and lung cancer screening have increased the detection of pure ground glass opacity (GGO) and mixed-density opacities. When these opacities are resected and then pathologically evaluated, they are classified according to the International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) classification of pulmonary adenocarcinomas [1]. This subclassification is based on studies showing that patients with small, peripheral, purely lepidic adenocarcinomas (adenocarcinoma in situ [AIS]) and those predominantly lepidic with invasion of 5 mm or less (minimally invasive adenocarcinoma [MIA]) have low recurrence rates and 5-year disease-free survival and overall survival approaching 100% [1–5]. This assessment, however, is determined by pathologists after resection, thus, limiting the surgeon's ability to preoperatively plan an appropriate resection.

The surgical planning for such lesions can be challenging. Because evidence suggests that some may be managed by sublobar resection, which provides comparable survival advantages and preserves pulmonary function compared with more aggressive cancers requiring lobectomy, the onus is on the surgeon to assess computed tomography (CT) images, anticipate the pathologic classification, and select the appropriate resection [6–9]. Even though numerous studies have demonstrated a correlation between CT images and the pathologic assessment, the utility of preoperative CT to guide the appropriate use of sublobar resection for indolent lesions has been controversial [10–12]. We sought to determine whether preoperative CT classification using a radiologic

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Acronyms and Abbreviations

AIS	= adenocarcinoma in situ
ATS	= American Thoracic Society
CT	= computed tomography
DFS	= disease-free survival
ERS	= European Respiratory Society
FNA	= fine needle aspiration
GGO	= ground glass opacity
IA	= invasive adenocarcinoma
IASLC	= International Association for the Study of Lung Cancer
IQR	= interquartile range
LVI	= lymphovascular invasion
MIA	= minimally invasive adenocarcinoma
OS	= overall survival
p	= pathologic
PET	= positron emission tomography
r	= radiologic
SUV	= standardized uptake value

version of the IASLC/ATS/ERS classification could guide decision making in the approach to the surgical resection of these lesions.

Patients and Methods

We performed a retrospective record and pathologic review from August 2001 to 2013 at the Swedish Cancer Institute. The study protocol was approved by the Swedish Medical Center Institutional Review Board and individual consent waived.

Study Population

Patients were selected from a prospectively collected pathology database and the Division of Thoracic Surgery database. Before 2011 patients were identified with the terms "bronchioloalveolar carcinoma" or adenocarcinoma with "bronchioloalveolar carcinoma" features. After the incorporation of the IASLC/ATS/ERS classification in 2011, the term "lepidic" on final pathologic assessment was used. We identified 187 patients who underwent resection of a dominant primary pulmonary lesion. The dominant lesion was defined as a lesion that was positive on positron emission tomography (PET), which is defined as a standardized uptake value exceeding 2.5, a lesion that was PET negative but had enlarged in total size or size of the solid component, or a lesion that was clinically suspicious for malignancy [13].

Reports for patients were reviewed and the following excluded: 4 with clinical N1/N2 disease, 5 with advanced disease, 7 with mucinous adenocarcinoma, and 12 with multiple synchronous primary tumors of different histology. Those patients with stable GGOs on CT in addition to the dominant lesion were included; however, only the dominant lesion was assessed. An additional 23 patients without radiographic images or pathology slides available for reevaluation were excluded, leaving 136 patients. The total tumor size was used to stage patients according to the TNM staging system.

Pathologic Classification

The dominant resected specimens were reevaluated by a lung pathologist (M.P.H.). The histologic type, tumor grade, lymphovascular invasion, bronchial margins, and pleural involvement were recorded. The total tumor and invasive component sizes were documented for histologic classification according to the IASLC/ATS/ERS classification into AIS, MIA, and IA [1]. The invasive component size was defined as the largest diameter of invasive adenocarcinoma in any focus in the lesion.

Radiologic Classification

To create a radiologic version of the IASCL/ATS/ERS classification system, the dominant lesion on the preoperative diagnostic CT scan was reevaluated by a thoracic radiologist (K.A.M.) blinded to the final pathologic assessment. The use of contrast and slice thickness was not mandated. The lobar location of the lesion, the location in the lung field divided into thirds (outer/middle/central), as well as the total tumor and solid component sizes in the axial dimension were documented. The diameter of the solid component was defined as the largest axial diameter of consolidation in the lesion on the lung window setting. This solid component on the CT image was substituted for the invasive component on the pathologic assessment.

Patients were classified using a radiologic classification system according to the following definitions: radiologic adenocarcinoma in situ (rAIS), total of 3 cm or less with no solid component; radiologic minimally invasive adenocarcinoma (rMIA), total of 3 cm or less with a solid component of 5 mm or less; or radiologic invasive adenocarcinoma (rIA), exceeding 3 cm total or a solid component exceeding 5 mm, or both.

Outcome Measures

To ascertain whether the radiologic classification system was successful, patient and tumor characteristics were compared against the established pathologic IASLC/ATS/ERS classification of the resected specimen [1]. Outcome measures included cancer recurrence, disease-free and overall survival, and radiologic-pathologic concordance.

Surgical Resection

Anatomic resections had systematic nodal sampling or comprehensive lymphadenectomy at the discretion of the surgeon. The mediastinum was preoperatively staged with mediastinoscopy or endobronchial ultrasound, or both, in selected cases. During segmentectomy, frozen section was used to confirm the absence of nodal metastases in hilar nodes. The resection type was defined by the final resection performed. An acceptable parenchymal surgical margin during sublobar resection was defined as at least equivalent to the tumor size and estimated at the operation.

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