Pure ground glass nodular adenocarcinomas: Are preoperative positron emission tomography/computed tomography and brain magnetic resonance imaging useful or necessary?

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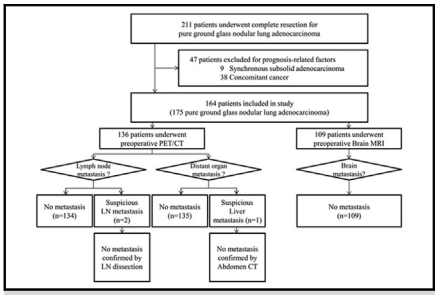
ABSTRACT

Objective: The utility of ^{18}F-Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) scanning and brain magnetic resonance imaging (MRI) as a staging workup for lung adenocarcinoma manifesting as pure ground glass opacity (GGO) is unknown. The purpose of this study was to determine the utility of these 2 tests for preoperative staging of pure GGO nodular lung adenocarcinoma.

Methods: The study included 164 patients (male:female, 73:91; mean age, 62 years) with pure GGO nodular lung adenocarcinoma who underwent PET/CT (in 136 patients) and/or brain MRI (in 109 patients) before surgery. Pathologic N staging and dedicated standard imaging or follow-up imaging findings for M staging were used as reference standards. The median follow-up time was 47.9 months.

Results: On PET/CT scan, abnormal FDG uptake of lymph nodes was found in 2 of 136 patients (1.5%); both were negative on final pathology. Abnormal FDG uptake of the liver was detected in 1 patient, which was also confirmed to be negative by dedicated abdominal CT. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of PET/CT in detecting metastases were not applicable, 98% (95% confidence interval [CI], 94%-100%), 0% (95% CI, 0%-71%), 100% (95% CI, 97%-100%), and 98% (95% CI, 94%-100%), respectively. No brain metastasis was found in preoperative brain MRI of 109 patients. Of 109 patients, 1 (0.9%) developed brain metastasis 30 months after surgical resection.

Conclusions: PET/CT and brain MRI is not necessary in the staging of pure GGO nodular lung adenocarcinoma. (J Thorac Cardiovasc Surg 2015;150:514-20)



Flow chart of patient enrollment and staging work-up for patients with pure ground glass opacity nodular lung adenocarcinomas.

Central Message

Patients with pure GGO adenocarcinomas had negative PET/CT and brain MRI. Unlike guidelines for NSCLC, these studies are unnecessary.

Perspective

The necessity of PET/CT and brain MRI in patients with GGO's are not determined. But, these are routinely practiced in patients with the adenocarcinoma manifesting as pure GGOs. We concluded that PET/CT and brain MRI add little utility in the staging of pure GGO adenocarcinoma regardless of tumor size. Our study can support the potential cost savings, as well as reduction of unnecessary radiation.

See Editorial Commentary page 521.

^{18}Fluorodeoxyglucose positron emission and computed tomography (FDG PET/CT) is recommended by the European Society of Thoracic Surgeons and American College of Chest Physicians for the preoperative (clinical) evaluation of mediastinal and distant metastases of patients with non–small cell lung cancer (NSCLS).[1,2] Despite the shortcomings of FDG PET/CT brain imaging, there are no recommendations for preoperative brain magnetic resonance imaging (MRI), even though the use of MRI is associated with better control of neurologic manifestations and longer survival.[3-5] Further uncertainty is added in those patients with the earliest of adenocarcinomas; that is, those manifesting as ground glass opacities (GGOs) although there are some guidelines for clinical T1a NSCLC or stage I NSCLC.[6-11] The purposes of our study were to assess the usefulness and necessity of FDG PET/CT and brain MRI in patients with GGOs and thus determine if these studies are mandatory in preoperative evaluations.

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Abbreviations and Acronyms

AIS = adenocarcinoma in situ
CT = computed tomography
FDG = fluorodeoxyglucose
GGN = ground glass opacity nodule
GGO = ground glass opacity
LN = lymph node
MIA = minimally invasive adenocarcinoma
MRI = magnetic resonance imaging
NSCLC = non–small cell lung cancer
PET = positron emission tomography
SUVmax = maximum standardized uptake value
TMN = tumor, node, and metastasis
VATS = video-assisted thoracoscopic surgery

PATIENTS AND METHODS

This retrospective study was approved by the institutional review board of Samsung Medical Center (Seoul, Republic of Korea), which waived the requirement for informed consent.

Patients

A total of 211 patients with histopathologically determined adenocarcinoma of the lung by complete surgical resection were enrolled from the thoracic surgery registry of NSCLC (October 2003-February 2014). The selection criteria for this study were available thin-section chest CT that indicated pure GGO nodules (GGNs) through the consensus review of 2 radiologists with 12 and 5 years' experience in chest CT, respectively, at the Samsung Medical Center. Pure GGNs were defined on chest CT scan because those composed purely of GGO on lung window images with no or barely identifiable soft-tissue attenuation within the lesion on mediastinal window images.

Of these 211 patients, 47 were excluded for the following reasons: 9 patients had concomitant solid or part solid adenocarcinoma in multiple nodules, including pure GGO nodular adenocarcinoma, and 38 had a previous or concurrent malignancy. Finally, 164 patients (male to female ratio, 73:91; mean age, 62 years) with pure GGO nodular lung adenocarcinoma who underwent contrast-enhanced CT before surgery were included in the analysis.

Characteristics of the Study Patients

Patient demographics and radiologic findings for the total study population are summarized in Table 1. Among the 164 patients, 175 GGNs (17 [10%] central location; 158 [90%] peripheral location) were identified on the screening chest CT performed at the time of initial operation. The median size of GGNs was 16.5 mm (range, 4-35 mm). Tumors that were larger than 30 mm were all negative for lymph node (LN) metastasis and distant metastasis. LN staging was determined using the pathologic results from video-assisted thoracoscopic surgery (VATS) (n = 105), thoracotomy (n = 6), and robot-assisted lobectomy (n = 2). The mean extracted LN station number per operation was 4.1, which were all pathologically negative of metastasis.

Of these 164 patients, imaging data were available for 136 who had FDG-PET/CT and 109 who had brain MRI before surgery (Figure 1). Twenty-eight patients did not undergo preoperative FDG-PET/CT; these patients had 31 pure GGNs. Among them, 28 pure GGNs (90%) were 2 cm or smaller, and the other 3 (10%) were ≤ 3 cm and clinical stage T1b lung cancer. Contrast-enhanced CT of these 28 patients revealed no LN enlargement. Therefore, for these 28 patients, metastasis determined using clinical and contrast-enhanced CT imaging studies served as the reference standard for determining the absence of metastasis. Fifty-five patients did not undergo brain MRI; 58 pure GGNs of these 55 patients were ≤3 cm in size and all were stage I lung adenocarcinoma. There was no evidence of LN metastasis or distant metastasis during the follow-up period (47.9 ± 23.1 months). Survival rate was 100%.

All pure GGNs except for 1 case were pathologic stage 1A. Pathologic tumor, node, and metastasis (TNM) staging was T1a to T3 N0 M0. The pathology is summarized in Table 2. Of 175 tumors in 164 patients, 34 were adenocarcinoma in situ (AIS) (19%), 54 were minimally invasive adenocarcinoma (MIA) (31%), and 87 were invasive adenocarcinoma (50%). The histologic subtypes, in decreasing order, were lepidic (69%), acinar (26%), and papillary (5%). All tumors were negative for lymphatic or vascular invasion. Even among nonlepidic adenocarcinoma subtypes such as acinar and papillary, there was no LN metastasis or distant metastasis. In 1 case the tumor invaded into the parietal pleura of the chest wall, and was TNM stage T3 and stage 2B (tumor size, 21.9 mm; histologic subtype, acinar predominant). LN metastasis or distant metastasis was not found in this patient.

Preoperative Staging with Imaging

The presence of LN metastases was evaluated using chest CT and FDG PET/CT. Metastases in other organs were determined by brain MRI and FDG PET/CT. All positive results were based on preoperative reports and also reviewed again retrospectively.

The following CT scanners were used in this study: a second-generation dual-source CT system (Somatom Definition Flash, Siemens Healthcare, Erlangen, Germany [7 studies]), a 64-MDCT scanner (Aquilion 64, Toshiba Medical Systems, Otawara, Japan [46 studies] or LightSpeed VCT, GE Healthcare [57 studies], Milwaukee, Wisc), a 40-MDCT scanner (Brilliance 40, Philips Healthcare, Best, The Netherlands [32 studies]), a 16-MDCT scanner (LightSpeed 16, GE Healthcare [36 studies] or LightSpeed QX/i, GE Healthcare [seven studies]), and an 8-MDCT scanner (LightSpeed Ultra, GE Healthcare [17 studies]). Unenhanced CT images were obtained with the following parameters: 120 kVp; 100 to 250 mA; beam pitch, 0.875 to 1.675; and section thickness, 0.75 to 2.5 mm for transverse. All imaging data were reconstructed with a bone (high-frequency) algorithm.

For FDG PET/CT scan, patients received an intravenous injection of 5.5 MBq/kg FDG and then rested for 60 minutes before scanning. Images were acquired using a PET-CT device (primarily a Discovery STe scanner; GE Healthcare), which included a PET scanner (2.5 minutes per frame in a 3-dimensional mode) and a 16-slice CT scanner.

Brain MRI was conducted using a 1.5-T and 3-T MRI scanner (Achieva; Philips Medical Systems, Best, the Netherlands) with a standard head coil. Three sequences were used for imaging: a T2W, axial, turbo spin-echo pulse sequence with fat suppression; a fluid-attenuation, inversion-recovery spin-echo sequence; and a noncontrast-enhanced and a contrast-enhanced T1W spin-echo sequence.

Two radiologists (with 12 and 5 years' experience in chest CT, respectively) evaluated the chest CT scans in consensus. LN assessment was based on LN size on the chest CT, with a short axis diameter > 10 mm defined as abnormal.[2] If mediastinal or hilar nodes showed high attenuation (>70 Hounsfield units) or benign calcification (eg, central nodular, laminated, popcorn, or diffuse) on unenhanced CT images, they were regarded as benign irrespective of their size.[12,13]

A chest radiologist with 5 years' experience in chest CT and a nuclear medicine physician with 20 years' experience of PET/CT interpretation evaluated the integrated FDG PET/CT images independently, and all decisions were reached in consensus. Both clinicians were unaware of the results of clinical and pathologic evaluation. On FDG PET/CT images, all LNs in the thorax with FDG uptake no greater than the normal background activity of the mediastinal blood pool (which had a maximum standardized uptake value [SUVmax] < 1.5, regardless of size) were considered cN0. An