Original Investigation

Modified Lung-RADS Improves Performance of Screening LDCT in a Population with High Prevalence of Non–smoking-related Lung Cancer

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Abbreviations and Acronyms

AAH atypical adenomatous hyperplasia
ACR American College of Radiology
AIS adenocarcinoma in situ
AUC area under the curve
GGN ground-glass nodule
PPV positive predictive value
Lung-RADS Lung Imaging Reporting and Data System
LDCT low-dose computed tomography
LR+ positive likelihood ratio
LR– negative likelihood ratio

Objectives: We proposed a modification of the ACR Lung Imaging Reporting and Data System (Lung-RADS) to clarify the characteristics of subsolid nodules with categories 1–11, and to compare the diagnostic accuracy with Lung-RADS and National Lung Screening Trial criteria in an Asian population with high prevalence of adenocarcinoma.

Methods: We analyzed a retrospective cohort of 1978 consecutive healthy subjects (72.8% nonsmoker) who underwent low-dose computed tomography from August 2013 to October 2014 (1084 men, 894 women). Lung-RADS categories 2 and 3 were modified to include subcategories of 2A/2B/2C and 3A/3B/3C, respectively. Clinical information and nodule characteristics were recorded. Receiver operating characteristic curves were used to compare diagnostic accuracy at different cutoffs.

Results: Thirty-two subjects (30 nonsmokers) had pathology-proven adenocarcinoma spectrum lesions in the follow-up period (1.6 ± 0.5 years). Modified Lung-RADS, using modified Lung-RADS category 2C as cutoff, had an area under the curve (AUC) of 0.973 in predicting adenocarcinoma spectrum lesions (sensitivity of 100%, specificity of 89.3%), which was significantly higher than that of Lung-RADS (AUC = 0.815, $P < .001$) and National Lung Screening Trial (AUC = 0.906, $P < .001$). Furthermore, modified Lung-RADS showed an AUC of 0.992 in predicting invasive adenocarcinoma (sensitivity of 95%, specificity of 97.8%) when category 3B was used as cutoff.

Conclusions: Modified Lung-RADS may substantially improve sensitivity while maintaining specificity for detection of adenocarcinoma spectrum lesions in an Asian population. Compared to Lung-RADS, it has enhanced ability to differentiate invasive from indolent adenocarcinoma by more refined subclassification of subsolid nodules using two cutoff values of category 2C and 3B. The effect of using modified Lung-RADS in clinical practice must be carefully studied in prospective large cohort studies.

Key Words: Screening; low-dose CT (LDCT); lung adenocarcinoma; diagnosis; sensitivity and specificity.

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NPV
negative predictive value

NLST
National Lung Screening Trial

MIA
minimally invasive adenocarcinoma

ROC
receiver operating characteristics

SSN
subsolid nodule

INTRODUCTION

The National Lung Screening Trial (NLST) demonstrated that annual lung screening of high-risk population with low-dose computed tomography (LDCT) results in a 20% reduction in lung cancer-specific mortality compared to screening with chest radiography (1). However, a major concern is the high false-positive rate of NLST by setting the cutoff threshold of positive scan at 4 mm for noncalcified lung nodule (2,3). In an effort to reduce false-positive rate and standardize reporting of lung cancer screening examinations, the American College of Radiology (ACR) in 2014 released the Lung Imaging Reporting and Data System (Lung-RADS) (4). Recent studies have demonstrated that Lung-RADS, compared to NLST criteria, substantially reduces the false-positive result rate with a small corresponding decrease in sensitivity (5,6).

In general, cancer cases that are falsely classified as negative by Lung-RADS and classified as positive screen based on NLST criteria are speculated to represent less aggressive lesions, such as minimally invasive adenocarcinoma (MIA) or adenocarcinoma in situ (AIS) (5). However, Lung-RADS was designed to be used in the United States where screening programs target high-risk smokers, and the diagnostic performance of Lung-RADS in populations with high prevalence of nonsmoking associated lung cancer, such as in China, Taiwan, Korea, and Japan, is unclear (7). Lung cancer is the leading cause of death among all cancer types in Taiwan, accounting for 19.7% of cancer mortality in 2012. In Taiwan, more than 95% of women with lung cancer are nonsmokers, and the majority of these patients have adenocarcinomas (about 83%) (8–10). More than half of women with lung cancer are diagnosed at advanced stages.

Given the significant differences in lung cancer demographics in Asia and the predominance of subsolid nodules (SSNs) and adenocarcinoma spectrum lesions, the criteria for lung cancer screening and the associated nodule classification and reporting systems require adjustments (6,7,11). Recent studies from Japan have also demonstrated a decrease in lung cancer mortality following the introduction of LDCT lung cancer screening in a community-based cohort (53.8% nonsmoker) (12). We proposed a modification of ACR Lung-RADS to be used in Asian populations with a high prevalence of adenocarcinoma spectrum lesions in mainly nonsmokers and compared its diagnostic accuracy to the ACR Lung-RADS and NLST criteria.

MATERIALS AND METHODS

Study Cohort

Institutional Review Board of Kaohsiung Veterans General Hospital in Taiwan approved this retrospective chart review and waived the requirement for informed consent because all images and follow-up data were obtained as part of routine clinical care. From August 2013 through October 2014, a total of 1978 consecutive asymptomatic participants underwent self-paid LDCT for lung cancer screening (1084 men, 894 women) at our institution. The inclusion criteria for subjects were ages between 40 and 80 years, absence of clinical symptoms, and willingness to participate in follow-up imaging or diagnostic workup. The exclusion criterion was a known history of lung cancer. Clinical information and demographic data, including a family history of lung cancer and other cancers in first- and second-degree relatives, past history of chronic obstructive pulmonary disease, and pulmonary mycobacterial infection (old and active), were recorded. Subjects were classified based on smoking status as current smokers, former smokers, and never smokers. For current and former smokers, a detailed smoking history including pack-years of smoking and the number of years since smoking cessation were also recorded. Diagnosis of lung cancer was retrospectively identified until August 31, 2015 from hospital-based cancer registry for all participants. Figure 1 shows the flowchart of the study.

LDCT Image Acquisition and Interpretation

All LDCT scans were performed with a 16- (Somatom Sensation 16, Siemens Healthcare, Erlangen, Germany) or a 64-slice multidetector computed tomography (CT) (Aquilion 64,Toshiba Medical Systems, Tokyo, Japan) in a low-dose setting from the lung apex to the lung base without intravenous or oral contrast enhancement (volumetric CT dose