



Association Between Sputum Atypia and Lung Cancer Risk in an Occupational Cohort in Yunnan, China*

Ya-Guang Fan, MD; Ping Hu, SM, ScD; Yong Jiang, MPH; Run-Sheng Chang, MD; Shu-Xiang Yao, MD; Wendy Wang, PhD; Jie He, MD; Philip Prorok, PhD; and You-Lin Qiao, MD, PhD

Background: Individuals with cytologic atypia in sputum may be at high risk for the development of lung cancer.

Methods: A prospective cohort study was conducted among occupational tin miners in Yunnan China based on an annual lung cancer screening program. Sputum samples were collected prospectively at baseline and the following seven annual screenings. The associations between risk factors and sputum cytology were analyzed by univariate and multivariate logistic regression. A proportional hazard model was used to analyze the association between the baseline sputum results and the incidence of lung cancer. The effect of consecutive sputum cytology on the increase of lung cancer risk was analyzed by logistic regression.

Results: Sputum cytologic atypia was associated with age, smoking, occupational radon and arsenic exposure, and asthma. Sputum cytologic atypia was an independent risk factor for lung cancer with an adjusted hazard ratio (HR) of 3.82 (95% confidence interval [CI], 2.82 to 5.18) in comparing normal to moderate or worse atypia. Compared to the lung cancer risk associated with normal sputum, the risk was significantly higher according to the degree of atypia for squamous carcinomas, small cell lung cancer and central lung cancer, with adjusted HRs of 5.70 (95% CI, 3.78 to 8.59), 3.32 (95% CI, 1.31 to 8.45), and 4.93 (95% CI, 3.51 to 6.92), respectively.

Conclusions: Sputum atypia is associated with an increased risk of lung cancer. Sputum cytologic examination combined with other screening examinations may play an important role in the early detection of lung cancer or in the selection of the optimal target population for more intensive lung cancer screening among this occupational cohort or similar population.

Trial registration: Clinicaltrials.gov Identifier: NCT00340405. (CHEST 2009; 135:778-785)

Key words: atypia; lung cancer; sputum; Yunnan, China

Abbreviations: CI = confidence interval; HR = hazard ratio; OR = odds ratio; Q = quartile; SCLC = small cell lung cancer; T0 to 3 = time 0 to 3; YTC = Yunnan Tin Corporation

Lung cancer is the most common cancer worldwide. In 2005 it was estimated that there were > 490,000 new cases of lung cancer in China.¹ Lung cancer is also a highly lethal disease; the 5-year survival rate for all stages combined is 15% in the United States.^{2,3} The reasons for the poor prognosis are late diagnosis and lack of effective treatment for symptomatic disease. In addition, the prognosis for lung cancer is related to the stage at which it is detected.⁴

Sputum cytologic examination as a lung cancer screening tool is not recommended by any organization for the general population or any high-risk

population.^{5,6} The reason is that prior screening trials⁷⁻⁹ have not shown a reduction of lung cancer mortality. Although low-dose CT is considered the most potentially effective screening tool, it may be insensitive to superficial, preinvasive cancers in the central airways that may be manifested in sputum.¹⁰ Therefore, biomarkers that might be identifiable in the sputum may complement radiologic imaging for lung cancer. In addition, lung cancer risk has been demonstrated to increase with increasing levels of sputum cytologic dysplasia, particularly at levels of moderate atypia or worse.¹¹⁻¹⁵

The aim of this study was to investigate whether sputum atypia can be used as a predictor of increased lung cancer risk among participants in an occupational cohort in Yunnan, China. Although annual chest radiography was also conducted, we focus our analyses in this report on the results from sputum cytology examinations.

MATERIALS AND METHODS

Study Design and Participants

The Yunnan Tin Corporation (YTC) study is a one-armed prospective cohort study initiated in 1992 with annual follow-up through 2001. Participants were tin miners in Yunnan, China and with at least 10 years of underground radon and/or arsenic exposure. Detailed inclusion criteria are presented elsewhere.¹⁶

At the time of enrollment, all participants completed standardized baseline questionnaires that included demographic characteristics; residential, occupational, smoking, and medical histories; and a dietary assessment component. From 1992 to 1999, a total of 9,295 eligible tin miners were enrolled in this study. Eight rounds of annual lung cancer screenings with chest radiography and sputum cytology were performed during this period. Among them, 9,084 participants underwent at least one sputum cytologic screening examination with adequate results. The YTC study received approval from the institutional review board, and informed consent was obtained for each participant.

Tobacco was consumed mainly in the form of cigarettes, water pipes, and Chinese long-stem pipes. The never-smoker was defined as having a smoking history of < 6 months. Screen-

detected cancers were defined as those diagnosed within 12 months of a positive screen. All other cancers were classified as interval cancers. Detailed definitions of occupational radon and arsenic exposures are given elsewhere.¹⁷ In this study, occupational radon and arsenic exposure were grouped into four quartiles (Q1 to Q4) based on each individual's cumulative radon or arsenic levels, respectively.

Sputum Collection: Processing and Interpretation

Sputum samples were collected either spontaneously or by an induction procedure, and stored at room temperature in Saccomanno preservative. Specimens were smeared on glass slides and stained with Papanicolaou stain for routine cytologic examination. Slides were independently screened by two cytopathologists from the Labor Protection Institute in the YTC. Sputum cytologic screening results were classified into degrees as follows: (1) 1 = negative; (2) 2-1 = slight atypical metaplasia; (3) 2-2 = moderate atypical metaplasia; (4) 2-3 = grave atypical metaplasia; (5) 3 = suspicious for cancer; (6) 4 = highly suspicious for cancer; (7) 5-1 = epidermoid carcinoma; (8) 5-2 = adenocarcinoma; (9) 5-3 = undifferentiated carcinoma (includes both large cell and small cell); and (10) other cancer. The positive cytology slides were defined as the screening results of degrees 2-3 and above, and reread by a confirmatory reader. In this article, we focus on moderate atypical metaplasia (degree 2-2) or worse (degrees > 2-2) to investigate whether sputum atypical metaplasia can be used as a predictor of lung cancer.

Statistical Methods

The associations between risk factors and sputum cytology results were analyzed by univariate and multivariate logistic regression.¹⁸ Person-years of follow-up were calculated from the date of the first sputum cytologic screening to the date of lung cancer diagnosis or lung cancer death or censoring as of December 31, 2001. The proportional hazards model was used to analyze the association between baseline sputum results and lung cancer incidence. The effect of consecutive sputum cytology on the increase of lung cancer risk was also analyzed by logistic regression.¹⁸ The Kruskal-Wallis test was used to compare participant age, radon and arsenic exposures. The χ^2 test of independence was used to evaluate the statistical significance of differences in proportions. All statistical tests were two-sided.

RESULTS

In this study, all analyses were restricted to the 9,084 participants who received at least one sputum cytology screening and had adequate results. Characteristics of the study participants are presented in Table 1. Most participants were men (93.9%), with women accounting for only 6.1% of participants. At the time of enrollment, 66.1% of participants were 40 to 59 years old. Of the participants, 23.9% never attended school, and 84.9% had a history of smoking. Table 1 also shows cumulative occupational arsenic and radon exposures and information on prior pulmonary diseases such as chronic bronchitis, asthma, and silicosis.

The association between personal/occupational characteristics and sputum cytology results in the baseline sputum screening is also given in Table 1.

*From the Department of Biology (Dr. Fan), Institute of Radiation Medicine, Chinese Academy of Medical Sciences, Tianjin, People's Republic of China; Department of Cancer Epidemiology (Drs. Jiang and Qiao), Cancer Institute, Chinese Academy of Medical Sciences, Beijing, People's Republic of China; Third People's Hospital of Honghe Autonomous District (Dr. Chang), Gejiu, Yunnan Province, People's Republic of China; Department of Epidemiology (Dr. Yao), Kunming Medical College, Kunming, Yunnan Province, People's Republic of China; Cancer Biomarkers Research Group (Dr. Wang), Division of Cancer Prevention, National Cancer Institute/National Institute of Health, Bethesda, MD; Cancer Institute (Dr. He), Chinese Academy of Medical Sciences, Beijing, People's Republic of China; and Biometry Research Group (Drs. Hu and Prorok), Divisions of Cancer Prevention, National Cancer Institute/National Institute of Health, Bethesda, MD.

None of the authors have any financial interests in the subject matter or any actual or potential conflicts of interest.

This study was supported by the National Cancer Institute/National Institutes of Health, grant No. 263-MQ-511694. This article describes an ancillary study for the National Cancer Institute project "The Study of Early Markers of Lung Cancer Among Tin Miners in Yunnan China," a federally funded registered clinical trial.

Manuscript received June 18, 2008; revision accepted September 16, 2008.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Ping Hu, SM, ScD, Mathematical Statistician, Biometry Research Group, Divisions of Cancer Prevention, National Cancer Institute/National Institute of Health, Executive Plaza North, Suite 3131, 6130 Executive Blvd, MSC 7354, Bethesda, MD 20892-7354; e-mail: ph107y@nih.gov
DOI: 10.1378/chest.08-1469

Download English Version:

<https://daneshyari.com/en/article/2903747>

Download Persian Version:

<https://daneshyari.com/article/2903747>

[Daneshyari.com](https://daneshyari.com)