

## Current Abstracts on Lung Cancer in Women

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**Title** Risk modification by CYP1A1 and GSTM1 polymorphisms in the association of environmental tobacco smoke and **lung cancer**: A case-control study in Japanese nonsmoking **women**.

**Source** International Journal of **Cancer**, 20 October, 2003, vol. 107, no. 1, p. 139-144, ISSN: 0020-7136.

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**Abstract** Genetic backgrounds may modify the association of environmental tobacco smoke (ETS) with **lung cancer** risk. Polymorphisms of both the activating and detoxifying enzymes, cytochrome P4501A1 (CYP1A1) and glutathione-S-transferase M1 (GSTM1), may be important as genetic factors. We conducted a multicenter case-control study in Japanese nonsmoking **women**. Cases were **women** aged 30-89 years and newly diagnosed as having **lung cancer** from November 1997 to March 2001 in 4 study areas. We also recruited age-matched (5-year strata) and hospital-matched nonsmoking controls. A total of 158 cases and 259 hospital controls supplied blood for genotyping. Detailed information on ETS exposure from husbands and that in other situations and on potential confounders was collected by interview. Odds ratios (ORs) were estimated by using conditional logistic models. We found no increase in the risk of **lung cancer** for CYP1A1 Msp I genotypes. For the GSTM1 null genotype vs. nonnull genotype, the OR was 1.37 (95% confidence interval (CI) 0.90-2.09), which indicated a somewhat increased risk for the GSTM1 null genotype. A gene-environment interaction was suggested, with combined GSTM1 null genotype and high-dose ETS exposure (gtoreq40 pack-years by husbands) conferring significantly higher risk (OR=2.27, 95% CI 1.13-4.57) compared to the GSTM1 nonnull genotype and low-dose ETS exposure (<40 pack-years). Our results do not support a major role of Msp I polymorphism of the CYP1A1 gene as a risk factor for **lung cancer** among nonsmoking **women**. In contrast, the GSTM1 null genotype posed an increased, although not significant, risk among them. Additional studies are warranted to confirm the ETS-GSTM1 polymorphism interaction suggested in our present study.

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**Title** Association between atherosclerosis and **female lung cancer**--a Danish cohort study.

**Source** **Lung cancer** {**Lung-Cancer**} 2003 Dec, VOL: 42 (3), P: 247-54, ISSN: 0169-5002.

**Abstract** Patients suffering from atherosclerotic diseases are prone to repeated episodes of ischemia/reperfusion that has been demonstrated to induce oxidative stress by formation of oxygen free radicals. It might therefore be expected that such endogenously exposure to free radicals increases the individual **cancer** risk in patients with atherosclerotic diseases. We therefore studied the sex-specific risk of **lung cancer** and other cancers in atherosclerotic patients in a prospective study conducted in the Copenhagen area. The study cohort was linked to the Danish Hospital Discharge Register and we identified 2261 1-year survivors of atherosclerotic diseases through 1977 and 1993, while 26150 of the study subjects had no record of an atherosclerotic diagnosis. After linkage to the Danish **Cancer** Registry associations between atherosclerosis and **cancer** were analysed for each sex separately by means of Cox proportional hazard regression models. Atherosclerotic **women** had a significant RR of **lung cancer** of 3.26 (95% CI: 1.95-5.46) compared to non-atherosclerotic **women** after adjustment for age, calendar period, study population, smoking habits, school education and alcohol consumption. No significant risk of male **lung cancer**, RR=1.12 (95% CI: 0.77-1.64), or other smoking-related cancers in either sex was observed after multivariate adjustment. Atherosclerosis did not predict non-smoking-related cancers in general in either men, RR=0.91 (95% CI 0.69-1.20), or **women**, RR=0.93 (95% CI: 0.64-1.35). We hypothesize that oxidative stress due to episodes of ischemia/reperfusion increases the risk of **lung cancer** in atherosclerotic females because of a gender specific susceptibility to oxidative DNA damage.

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**Title** Menopausal effects on presentation, treatment, and survival of **women** with non-small cell **lung cancer**.

**Source** The Annals of thoracic surgery {Ann-Thorac-Surg} 2003 Dec, VOL: 76 (6) , P: 1789-95, ISSN: 0003-4975.

**Abstract** BACKGROUND: Small population studies have reported higher survival rates for **women** than men with non-small cell **lung** carcinoma (NSCLC). Because human NSCLC cells express estrogen receptors, we evaluated hormonally active and inactive **women** to identify biologically mediated differences. METHODS: A total of 14,676 US **women** with stage I through IV primary non-small cell **lung cancer** (NSCLC) from the 1992 to 1997 Surveillance, Epidemiology, and End Results database were grouped into two categories based on the average menopausal age of 51 years as defined by the American College of Obstetricians and Gynecologists: ages 31 to 50 premenopausal (n = 2,230, 15%) and ages 51 to 70 postmenopausal (n = 12,446, 85%). Extreme ages were excluded. Statistics were calculated with chi(2) or Mann-Whitney tests, Kaplan-Meier estimates with log-rank tests, and Cox proportional hazards models. RESULTS: Premenopausal **women** more commonly presented with advanced clinical stage, less favorable histology (adenocarcinoma), and poorly differentiated tumors, and more often

underwent pneumonectomies. Surgery with curative intent was performed in 31% premenopausal and 33% postmenopausal **women** ( $p = 0.03$ ). Overall survival for premenopausal and postmenopausal **women** was not significantly different (median 10 and 9 months, all stages; 70 and 71 months, stages I and II). Adjusting for significant covariates (stage, histology, size, grade, extent of surgery), postmenopausal **women** had higher **lung-cancer-related** deaths (hazard ratio, 1.14; 95% confidence interval, 1.03 to 1.27). CONCLUSIONS: Premenopausal **women** presented more often with advanced disease and underwent more extensive resection, yet had survival advantage after covariate adjustment. Additionally, postmenopausal **women** had a survival advantage compared with their male counterparts. Results suggest that estrogen exposure creates a milieu that may confer a protective effect through some yet unknown mechanisms that determine outcome of the neoplastic process and warrant further investigation.

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**Title** Changes in body composition in men and **women** with advanced nonsmall cell **lung cancer** (NSCLC) undergoing chemotherapy.

**Source** Journal of Human Nutrition and Dietetics, October 2003, vol. 16, no. 5, p. 323-326, ISSN: 0952-3871.

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**Abstract** Background: Men with nonsmall cell **lung cancer** (NSCLC) are more susceptible to weight loss than **women**. The composition and aetiology of these gender specific weight changes are not known. Methods: Measurements of body mass, body composition and energy balance (resting energy expenditure and energy intake) were made in 15 men and six **women** before and after chemotherapy for NSCLC. Results: Over the course of chemotherapy minimal weight change was observed in both men and **women**. Men increased body fat from 25.0 $\pm$ 5.5 to 27.9 $\pm$ 7.9% ( $P < 0.05$ ) whereas fat free mass (FFM) tended to decrease ( $P = 0.063$ ). There was no change in body fat or FFM in the **women**. In the men resting energy expenditure decreased over the course of chemotherapy from 113.2 $\pm$ 15.9 to 105.1 $\pm$ 10.1% of the value predicted from the Harris Benedict equation ( $P < 0.05$ ). In the **women** resting energy expenditure (REE) did not alter. Conclusion: Over the course of chemotherapy for NSCLC, men and **women** appear to have different patterns of change in body composition and in energy expenditure.

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**Title** Pretreatment with 8-methoxypsoralen, a potent human CYP2A6 inhibitor, strongly inhibits **lung** tumorigenesis induced by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in **female** A/J mice.

**Source** Cancer Research, November 15, 2003, vol. 63, no. 22, p. 7581-7583, ISSN: 0008-5472 (ISSN print).

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**Abstract** Human CYP2A6 has been recognized as being involved in the mutagenic activation of promutagens such as the tobacco-specific nitrosamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). Methoxsalen (8-methoxypsoralen) was reported to inhibit CYP2A6. In the present study, the inhibitory effects of methoxsalen on NNK-induced **lung** tumorigenesis in **female** A/J mice were examined. **Female** A/J mice were treated with methoxsalen at doses of 50 or 12.5 mg/kg body weight, given by stomach tube, daily for 3 days. One h after the final treatment, NNK was injected i.p. at a dose of 2 mg/mouse. The experiments were terminated 16 weeks after the first methoxsalen treatment, and **lung** adenomas were analyzed. Pretreatment of methoxsalen significantly reduced tumor incidence from 93.8% to 16.7% (50 mg/kg) and 20.0% (12.5 mg/kg), and tumor multiplicity from 5.97 to 0.23 (50 mg/kg) and 0.25 (12.5 mg/kg) tumors/mouse. These results clearly demonstrated that methoxsalen, a potent human CYP2A6 inhibitor, is a strong chemopreventive agent against NNK-induction of **lung** tumorigenesis.

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**Title** Adenocarcinoma of the **lung** among **women**: risk associated with smoking, prior **lung** disease, diet and menstrual and pregnancy history.

**Source** Lung cancer {**Lung-Cancer**} 2003 Sep, VOL: 41 (3), P: 283-93, ISSN: 0169-5002.

**Abstract** To investigate the role of tobacco and some other known or suspected factors responsible for the risk of developing adenocarcinoma of the **lung**, and to compare with other cell types (squamous-, small- and large-cell cancers) in Czech **women**, we conducted a case-control study. Data collected by personal interviews from 145 cases of adenocarcinoma of the **lung**, 221 **lung** cancer cases of other cell types, and 1624 controls were analyzed using unconditional logistic regression. Cigarette smoking was the main determinant of all major cell types of **lung** cancer among Czech **women**, its effect was weaker on adenocarcinoma than on squamous-, small- and large-cell cancers. Among never smokers, passive smoking in childhood (before age 16) did not significantly increase the risk of adenocarcinoma (OR=1.35, 95%CI 0.75-2.45), contrasting with an elevation in the risk of squamous-, small- and large-cell cancers combined (OR=2.10, 95%CI 1.02-4.33). Excess risk associated with consumption of red meat daily or several times per week (OR=1.81, 95%CI 1.04-3.18) was restricted to squamous-, small- and large-cell cancers combined. Wine drinking, at higher frequency than once per month, was inversely associated with the risk of adenocarcinoma (OR=0.46, 95%CI 0.23-0.92), however, not with squamous-, small- and large-cell cancers combined (OR=0.77, 95%CI 0.47-1.28). Inverse associations with the risk of squamous-, small- and large-cell cancers combined emerged for the quantity of menstrual flow (OR=0.63, 95%CI 0.40-0.99), and pains or mental tension related to menses (OR=0.61, 95%CI 0.42-0.89).

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**Title** K-ras mutations in **lung** carcinomas from nonsmoking **women** exposed to unvented coal smoke in China.

**Source** Lung cancer {**Lung-Cancer**} 2003 Jul, VOL: 41 (1), P: 21-7, ISSN: 0169-5002.

**Abstract** Lung cancer mortality rate in nonsmoking **women** in Xuan Wei (XW) County is the highest in China. The XW **lung** cancer rate is associated with exposure to coal smoke, containing high concentrations of polycyclic aromatic hydrocarbons (PAHs), in unvented homes. Here we investigated codon 12 K-ras mutations in **lung** tumors or sputum samples from 102 XW **lung** cancer patients (41 nonsmoking **women** and 61 smoking men). In addition, we analyzed specimens from 50 **lung** cancer patients (14 nonsmoking **women**, 33 smoking men and three nonsmoking men), from Beijing and Henan (B&H), where natural gas is the main domestic fuel. K-ras mutations were found in nine **women** (21.9%) and 14 men (22.9%) from XW, with G to T transversions accounting for 66.7 and 85.7%, respectively. Among B&H patients, one woman (7.1%) and six men (16.7%) had K-ras mutations, with G to T transversions accounting for 66.7% of the mutations in the men. Therefore, the frequency and type of K-ras mutations in XW nonsmoking **women** are similar to those of K-ras mutations found in both XW and B&H smoking men. On the other hand, the mutation frequency in XW **women** is higher than, although not statistically significant from, that in the B&H nonsmoking **women** ( $P=0.28$ , two-sided Fisher's Exact Test). These results suggest an association between exposure to coal smoke and the increased K-ras mutation frequency in XW nonsmoking **female lung** cancer patients. They also suggest that the mutagens and/or mechanisms of mutations in these nonsmoking **women** are similar to those responsible for K-ras mutations in cigarette smoking **lung** cancer patients, which are probably induced largely by chemicals such as PAHs.