Lung Cancer in Chinese Women--Varying Risk Factors by Ethnicity and Climate

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A review of published epidemiological studies on lung cancer consistently shows Chinese females in China, Hawaii, Hong Kong, Singapore, and Taiwan having low relative (2-4) and attributable risks (-1/3) from smoking. However, female lung cancer incidence/mortality rates within China are variable, with some comparable to the lowest rates in other parts of the world. This variability suggests the role of environmental etiological factors. Research on risks from inhaled air pollutants indicate that smoky coal used for cooking and heating in the colder parts of NE and SW China increased risk for lung cancer. However, risks from other air pollutants like environmental tobacco smoke, cooking fumes, and cooking oils were equivocal, and that for mosquito coil, incense, and other cooking fuels showed no risk. Risk from the effects of diet are inconsistent, with some studies from China showing increased fruit and vegetable intakes associated with increased risk. However, dietary results from Chinese communities outside China (Hong Kong, Singapore, Taiwan) are more similar to risks found among Western societies. There was some indication that previous respiratory diseases like chronic bronchitis and tuberculosis may be associated with lung cancer risk, but these results may be due to prodromal symptoms and recall bias, respectively. The role of reproductive health factors like parity, age at menopause, menstrual cycle length, etc. is unclear. Hence, aside from smoky coal exposure in cold and less developed parts of China, the etiological factors causing high lung cancer rates among Chinese women living in affluent urban warm climates like Shanghai, Hong Kong, Singapore, and USA remain unclear. J Epidemiol, 1996; 6: S231-S236.

Research over the last 25 years has confirmed the unusual phenomenon of high rates of unrelated to smoking lung cancer among Chinese women living in overseas communities and certain areas in China. Table 1 shows the world age-adjusted incidence rates of Chinese females living in 7 different communities for the period 1983-71). Female lung cancer incidence rates per 100,000 varied from a low of 11.2 in Qidong City to a high of 33.2 in Tianjin and 32.6 in Hong Kong. Qidong City, a small city of 1.3 million, is just north of Shanghai (population 12 million) and shares a common Jiangsu Province cultural area with Shanghai. Yet Qidong's incidence rates are relatively low, comparable to that of Osaka at 11.7/100,000 or Miyagi at 11.0/100,00010.

Is it Inherited or Environmentally Induced?

Further evidence from health statistics suggests that environmental rather than racial inherited factors play a pivotal role in the high incidence rates among Chinese women in some communities. From a nation-wide survey of cancer mortality in China from 1973-5, world age-adjusted female lung cancer mortality rates per 100,000 varied from a low of 1.6 in Gansu Province to the highest level of 14.3 in Shanghai8. Data on mortality trends in Hong Kong from the cancer registry indicates that female lung cancer deaths trebled from 7.7 in 1961 to 23.0 in 19918. Moreover, the lung cancer mortality rate of Chinese females from Guangdong Province in China, the origins of most Cantonese Chinese in Hong Kong and just across the border from Hong Kong, was only 2.9 for the period 1973-58. And finally, migrant studies of Chinese females in the USA...
show that first generation migrants had age adjusted mortality rates per 100,000 of 23.5, second generation of 15.4, and Chinese in China of 5.7. Hence the large range in mortality rates from within China, the trebling of mortality rates in Hong Kong over 30 years, the 8 times higher mortality in Hong Kong vs. Guangdong, China, and the 3-4 times higher mortality among Chinese migrants to the USA vs. China would suggest environmental over genetic factors for etiology.

INHALED RISK FACTORS

A review of published findings concerning various risk agents shall be critically summarized below. For case-control studies, results that used population rather than hospital controls will be preferred. For other findings, relative risks (RR) with 95% confidence intervals (CI) that adjusted or accounted for demographic factors (e.g. age and socio-economic status) and smoking were also preferred. Little reliability was placed on RR that were derived from cells containing fewer than 5 subjects. Statistical significance was defined as p ≤ 0.05.

Smoking

From a review of published reports on lung cancer and smoking, some 70-90% of European and North American female lung cancer patients reported a previous history of smoking compared with only 22-56% for Chinese women. A combined analysis of 8 case-control studies conducted in China estimated the overall attributable risk (AR) from smoking to be 26% and the RR 2.3. Similarly, for Hong Kong women the AR is 36% and RR is 2.8, for Singapore women the RR is 3.6, and for Chinese women in Hawaii the AR is 11% and RR 1.8. Moreover, a comparative study of lung cancer incidence rates not attributable to smoking for different ethnic groups living in Pacific Basin countries found that Japanese, White, and Hawaiian females had rates ranging from 7.3 to 7.5/100,000 but rates for Chinese women living in Hong Kong, Shanghai, and Taiwan were more than twice as high at 15.2, 18.4, and 20.5 respectively. Hence epidemiological studies have consistently shown that Chinese women compared to women of other ethnic backgrounds, have relatively low RR and AR from smoking, but high incidence rates of lung cancer unrelated to smoking.

Environmental Tobacco Smoke

Studies in Hong Kong, Shanghai, and Taiwan have not consistently found increased risks from environmental tobacco smoke, usually defined as a wife living with a smoking husband or being exposed during childhood. Chinese women do not have exceptionally high levels of exposure, as suggested by an international study of urinary cotinine levels (a metabolite of nicotine) among women in 10 countries and 13 sites. From the 13 sampled populations, Shanghai women's levels were the lowest and that for Hong Kong ranked fourth highest, although Hong Kong's levels were artifactually high due to low creatinine levels. However, a case-control study among women in northeast China found that wives with smoking husbands had significantly reduced risk for lung cancer (RR 0.7, 95% CI 0.6-0.9) which the authors explained as may have been obscured by exposure to other air pollutants.

Coal Smoke

In the warmer climate of Hong Kong, Shanghai, and Taiwan no increased risk from coal smoke was found. However, studies on Chinese women living in colder climates like NE and mountainous SW China have found increased lung cancer risk from the use of smoky coal for heating and cooking. From the NE region of Harbin and Shenyang, the RR from use of burning 'kangs' (a bed heated by coals) was 1.5 (1.1-2.0) and coal stoves was 1.3 (1.0-1.7). From the rural mountainous area of Xuan Wei, Yunnan Province in SW China, the RR associated with smoky coal use was estimated to be about 2.6. Analysis of air particles from indoor coal combustion in Xuan Wei have identified large concentrations of polycyclic aromatic hydrocarbons (PAH), many of which are mutagenic and carcinogenic. The use of coal heaters and stoves in poorly ventilated rooms that may get so smoky that visibility is only a few feet, seems a likely risk factor for Chinese women living under those conditions.

Mosquito Coil and Incense Smoke

Studies from Chinese women living in the tropical/subtropical areas of Singapore, Hong Kong, and Taiwan where mosquito coils are commonly burned, have not found statistically significant increased risks from their usage, although they are a source of airborne PAH.

Incense, another source of domestic PAH, is also popularly burned in these three areas for religious and ancestral worship. In the Singapore study no statistically significant increase was associated with incense burning among women, although for both males and females who used incense while sleeping the RR was 4.11 (p<0.01), but this was only based on 14 cases and 5 controls. In the Taiwan study of men and women, increased incense burning was associated with reduced risk for adenocarcinoma such that those who burned it 14+ times/week had RR of 0.24 (0.10-0.60). Similarly in Hong Kong, increasing years of exposure to incense was associated with reduced risk, with RR of 0.5 (0.03-0.81) at the highest level of 40-70 years, but this was only found among women who had smoked (with adjustment for lifetime tobacco consumption). Nonsmoking Hong Kong Chinese women were unaffected. For the Hong Kong data, these results were partially explained by the healthier diets of female smokers who burned incense vs. those who did not, with the significant dietary intake items being similar to those associated with
reduced risk for lung cancer.  

**Air Pollutants from Cooking**

MacLennan et al. was among the first to explore whether Chinese cooking methods might explain the high risk of lung cancer among Chinese women. At least 3 factors have been researched: type of fuel used; frequency/duration of exposure to cooking fumes from stir-frying, deep frying, etc.; and the type of cooking oil that is used.

The use of coal as a cooking fuel was already identified as a significant risk factor for women living in NE and SW China. A study in Taiwan estimated a RR of 24.3 (3.0-199.5) from the use of coal as a cooking fuel among men and women with squamous and small cell lung cancer, but this estimation is unstable because it was based on 10 cases and 2 controls. No association with cooking fuel type and lung cancer was found in Shanghai and Singapore. Although a RR of 1.6 (p=0.02) was associated in Hong Kong with kerosene stoves, the authors believed that this reflected the lower socio-economic circumstances of cases rather than lung cancer risk because kerosene is a cheaper fuel than liquid petroleum gas.

Four studies on exposure to cooking fumes had inconsistent results. Investigations in Taiwan on frying, stir-frying, etc., found no significant RR. Similarly, no increased risks from cooking were identified in the Singapore study. Among Shanghai women, more frequent stir-frying was associated with a RR of 2.6 (1.3-5.0), and that for boiling a RR of 2.2 (1.3-3.7). However, there was no significant risk from deep frying with a RR of 1.9 (0.5-6.8) although a study among women in NE China found a RR of 1.9 (1.4-2.7) from increasing monthly frequency of deep frying. Among Hong Kong women who had never smoked, increasing years of cooking was associated with a significant reduction in risk with RR 0.37 (0.14-0.96) for those who had cooked 41+ years compared to those at the lowest tertile of 0-25 years. The Hong Kong results could have been due to the poorer diets associated with female controls who cooked for > 25 years compared to those ≤ 25 years.

Two studies investigated cooking oils. The Shanghai study found that women who used rapeseed oil rather than soybean oil had RR 1.4 (1.1-1.8). However, this study did not adjust for income, and rapeseed oil is a less fragrant and cheaper oil compared to soybean oil in Shanghai. Further chemical analysis of cooking oils has shown that heated rapeseed oil from China contains more mutagens that its US counterpart (canola oil) because of higher levels of impurities.

The influence of socio-economic factors may also explain the Hong Kong findings that never-smoked women who did not use corn oil for cooking had a RR of 2.7 (1.1-6.2). During the period when the subjects were studied, 1981-3, corn oil was advertised as being a "healthy choice" because of its high levels of polyunsaturated fats that were purported to be good for preventing heart disease. Traditionally, the cooking oil of choice was peanut oil because of its fragrance and achievable high temperature which would seal-in the juices of stir-fried foods. Price-wise, the cost of peanut and corn oil were similar, with rapeseed oil a much cheaper oil used by poorer households. Hence, the Hong Kong study interpreted the low risk from corn oil as reflecting a household's attitude in modifying cooking behavior for health benefits rather than for reasons of the palate.

**INGESTED RISK FACTORS**

**Fruit and Vegetables**

There was no consistent direction from the effects of consuming more vegetables/fruit or their micronutrients, carotenoids, among the four populations of Chinese women where this was studied. For analysis of men and women with higher vegetable consumption, Singapore's RR was 0.45 (0.3-0.7), and Taiwan's RR was 0.47 (0.23-0.99). However, no effect from vegetable consumption was found for women in Hong Kong or NE China. On the other hand, women in Shanghai who ate more carotene rich foods had an increased risk of 2.0 (1.67-3.33). Similarly, contradictory results were found for higher fruit consumption, with Hong Kong's women having a RR of 0.42 (0.19-0.92), but NE Chinese women having a RR of 1.5 (1.2-2.0).

**Meat, Fish, and Alcohol**

Among women in NE China, lung cancer risk from increased consumption of animal protein had a RR of 2.3 (1.7-3.0) and that for alcohol a RR of 1.3 (1.0-1.8). Similarly in Hong Kong, alcohol consumption was associated with a RR of 1.9 (0.9-3.7) although it was of borderline significance with trend p-value at 0.076. The Hong Kong study of never-smoked women also found more fresh fish to be protective with RR of 0.4 (0.2-0.8), but increased consumption of smoked meats/poultry were suggestive of higher risk for squamous and small cell lung cancers with RR of 1.7 and trend p-value at 0.06. However, women's risk in Shanghai were unaffected by retinol rich foods like fish, liver, or eggs.

These results show that there is no consistency in the direction or effects of diet on lung cancer risk among Chinese women. The patterns among women in more economically developed areas like Taiwan, Singapore, and Hong Kong are more similar to that found in Western countries, where fruit and vegetables may be protective of cancer. However, the significantly higher risks associated with increasing fruit consumption in NE China, and vegetable consumption in Shanghai may reflect their lower socio-economic development where fruit and vegetables are relatively cheap and more likely to be eaten by the poor. It is notable that both the NE China
and Shanghai studies made no statistical adjustments for income. Both adjusted for education, but with the economic reforms of post 1949 communist China still moderately intact at that time (mid-1980’s), education would not be a good indicator of income or social status.

**OTHER RISK FACTORS**

**Reproductive Health Factors**

Studies on the risk relationship of various measures of reproductive health have had mixed results. In NE China, older age at natural menopause (55+) was associated with a RR of 1.7 (1.0-3.2) and having a history of miscarriage a RR of 1.5 (1.2-1.8)\(^{18}\). Shanghai women with adenocarcinoma also had a higher RR of 1.3 (0.9-1.7) for natural menopause at age 50+, and shorter menstrual cycle length with RR 2.9 (1.5-5.7)\(^{10}\).

However, Hong Kong women who had never-smoked had no risk relationships from menopausal age or number of miscarriages (not published). They had significantly reduced risk from increasing live births, such that smaller household size was associated with RR 2.4 (1.0-5.6)\(^{20}\) and measurements of parity were treated as a confounder in the logistic models of analysis for other variables.

**History of Lung Diseases**

Among women in NE China, chronic bronchitis /emphysema was associated with a RR of 1.4 (1.2-1.8) and pneumonia with RR 2.1 (1.3-3.3)\(^{18}\). Women in Shanghai had RR of 1.7 (1.1-2.4) for tuberculosis, RR of 1.9 (1.2-3.0) for pneumonia, and RR of 2.0 (1.0-3.7) for emphysema, but no significant increase from chronic bronchitis without emphysema\(^{10}\). Taiwan's analysis of men and women with squamous or small cell lung cancers had RR of 4.5 (0.9-22.3) for chronic bronchitis and RR 6.7 (0.97-46.1) for tuberculosis\(^{10}\). Among never-smoked Hong Kong Chinese women, chronic bronchitis was associated with increased RR of 2.0 (trend p=0.02).

These results of risk from previous lung diseases are more consistent, in the sense that the direction of the risk was generally higher if significant risks were found. However, recall bias may be an uncorrectable problem in such findings because of the natural tendency of lung cancer patients to spend more time to recall previous lung diseases than healthy controls [because of the lay tendency to believe that they are etiologically related]. Moreover, symptoms of chronic bronchitis, i.e. cough and phlegm, may be prodromal symptoms of lung cancer.

**CONCLUSION**

A review of published studies on lung cancer among Chinese women living in various parts of China and overseas communities confirms that their attributable risks and relative risks from smoking are relatively low when compared to Western women. There is some variation by place, but overall approximately 2/3 of the cases of lung cancer are not attributable to smoking, and the RR from smoking ranges from 2 to 4. The absolute incidence/mortality rates, however, are more variable, with communities not in mainland China (Singapore, Hawaii, Hong Kong) especially those of Cantonese origin\(^{9,20}\) having high incidence rates, and some large metropolitan cities within China (Tianjin, Shanghai) having high rates. However, other cities within China like Qidong and rural provinces like Gansu have low mortality rates that are comparable to populations elsewhere. These variations, and the fact that lung cancer was found to rapidly increase within recent decades in Hong Kong and Singapore, would suggest that Chinese women are not genetically predisposed to having lung cancer.

The primary suspicion in the etiology of respiratory cancers is inhaled pollutants. For environmental tobacco smoke, contradictory results were found, with women in NE China having reduced risk of 0.7, and those from Shanghai an increased RR of 1.7. Yet an international survey of urinary cotinine levels in 10 countries and 13 sites had Shanghai women having the lowest levels of exposure. Hence, the associations (either way) may be more indicative of other factors associated with a smoking husband than the smoke that emanates from his cigarettes.

Other air pollutants like smoke from burning incense or mosquito coils had no effects on lung cancer risk. However, in the colder climate areas of NE and SW China, where smoky coal is used for cooking and heating under unventilated conditions, risk from exposure ranged from 1.3 to 2.6. Other studies investigating air pollutants from cooking oil type and exposure to fumes from stir-frying resulted in no consistent pattern of risk.

Similarly, the results of ingestaed foods lacked consistency in direction of risk. There was a tendency for women outside mainland China (Hong Kong, Singapore, Taiwan) to have dietary risk patterns more similar to that found in Western populations, i.e. fruit and vegetables may be protective. This may reflect their higher level of economic development and Westernization so that dietary correlates of smoking and income are more similar to that found in Western societies. However, in Shanghai, greater vegetable consumption was associated with increased risk, and in NE China greater fruit consumption was associated with increased risk. These results may be due to the confounding effects of income, which was not an adjusted variable in those studies.

There was also no pattern emerging concerning reproductive health indices like childbirth, age at menopause, miscarriages, etc. There was a tendency for increased risks from past lung diseases like chronic bronchitis, pneumonia, and tuberculosis, but these results may be due to recall bias from patients, and chronic bronchitis acting as a prodromal symptom of lung cancer.
Table 1. Chinese Female Lung Cancer Incidence.

| Location            | Incidence |
|---------------------|-----------|
| Qidong City, China  | 11.2      |
| Shanghai, China     | 18.1      |
| Los Angeles, USA    | 18.2      |
| Hawaii, USA         | 18.4      |
| Singapore, Chinese  | 21.9      |
| Hong Kong           | 32.6      |
| Tianjin, China      | 33.2      |

World Age-Adjusted Rates 1983-7(1)

In conclusion, the non-smoking related risk factors for lung cancer among Chinese women may vary by where they live and ethnic backgrounds. Fumes from smoky coal seem to be a risk factor for women who live in poor and unventilated homes in cold climates in China, whereas dietary, cooking, or other unidentified factors may be affecting women living in affluent urban and overseas Chinese communities.

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