MAYO CLINIC
Cancer Center

Volume 2

Lung Cancer Research Update

Warmest greetings from the staff of the Mayo Clinic Lung Cancer Research Program

Over the past seven years, thousands of lung cancer patients and their relatives have taken part in our study. Their efforts and those of our research team have led to three national grant awards for research and many published scientific papers. These achievements would not have been possible without your support. Therefore, all of us who work in lung cancer research at Mayo Clinic wish to thank all of you.

The purpose of this research update is to let you know about the progress of our research activities and recent publications. We believe that communication between you and the research team is very important. The success of our ongoing research program depends upon people like you and your family members. Through this newsletter, we hope to achieve two main goals: 1) inform you of what we have learned about lung cancer and 2) encourage you to continue to take part in our ongoing research.

Progress of our major research projects

Our study team is studying the causes of lung cancer, as well as patient outcomes. Our basic aims are to find people who are at high risk of developing lung cancer through better understanding of how genes and the environment interact, to diagnose lung cancer at an early and curable stage, to find a group of genes or traits that can be easily tested to guide treatment for each patient, and to improve survival and quality of life among lung cancer patients.

Project 1

Updated Data on Chances of Surviving Lung Cancer Over Time

Lung cancer will continue to be a very important medical and public health problem for some time. Very little improvement has been made on how to cure the disease, particularly in patients with advanced disease. To better understand the causes and natural history of lung cancer, we need to study the changes over time of how the disease occurs and what is likely to happen to newly diagnosed patients.

To do so, we studied the medical features and survival time of 5,628 new lung cancer patients who were diagnosed between 1997 and 2002. Of these patients, 58% were men with an average age at diagnosis of 66 years, and 42% were women with an average age at diagnosis of 64. Ten percent were younger than 50 years of age and 8% were older than 80 years of age at the time of diagnosis. The estimated five-year survival rate of patients with non-small cell lung cancer (NSCLC) was 66% for stage IA; 53% for stage IB; 42% for stage IIA; 36% for stage IIB; 10% for stage IIIA; 12% for stage IIIB; and 4% for stage IV. The five-year survival of patients with small cell lung cancer was 22% for early-stage and 1% for late-stage disease. We concluded that

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Project 1 (continued)

survival of lung cancer patients in our study was slightly improved compared to earlier reports, particularly for stages IIIB and IV non-small cell lung cancer. These results will be published in 2005 in the journal, *Chest*.

Gender has been reported as a predictor for NSCLC outcomes. However, most of the previous reports were limited to selected groups of patients. The impact of gender on NSCLC survival across disease stage, tumor cell type, and therapies needs to be further studied. From our patient group, we observed that more men smoked, and men were heavier smokers than women; no difference was found in cancer stage and treatment between genders; and men were at a 20% higher risk of dying compared to women following a diagnosis of NSCLC. These findings are published in the journal, *Annals of Thoracic Surgery*.

Yang P, Allen MS, Aubry MC, et al. Clinical Features of 5,628 Primary Lung Cancer Patients: Experience at Mayo Clinic, 1997-2003. Chest 2005

Visbal AL, Williams BA, Nichols FC, et al. Gender Differences in Non-Small Cell Lung Cancer Survival: An Analysis of 4,618 Patients Diagnosed Between 1997-2002. Ann Thorac Surg 2004; 78(1):209-215

Project 2 Quality of Life of Patients Who Survive Lung Cancer

Evaluation of patients' self-reported health status and quality of life (QOL) is very important in the study of diseases such as lung cancer. These patients can be treated by many prescribed methods that have similar curative results; and therefore, the QOL view is becoming more important.

We reported the findings of a QOL assessment performed with the current version of the Lung Cancer Symptom Scale questionnaire in a group of 650 patients with lung cancer. A significantly better overall QOL was observed among women and among patients with early-stage disease. No significant differences in overall QOL were observed when age or marital status were considered.

To further describe how cigarette smoking and QOL are related in lung cancer survivors, information provided by 1,506 patients was analyzed. At the time of lung cancer diagnosis, 18% of patients were never-smokers, 58% were former smokers and 24% were current smokers. Thirty percent of current smokers, at the time of diagnosis continued to smoke at the time of follow-up (i.e., persistent smokers). Six of the individual QOL components (appetite, fatigue, cough, shortness of breath, lung cancer symptoms, and illness affecting normal activities) and overall QOL were better among those who never smoked than among persistent smokers. Former smokers had intermediate QOL scores.

Garces YI, Yang P, Parkinson J, et al. The Relationship Between Cigarette Smoking and Quality of Life after Lung Cancer Diagnosis. Chest 2004:126(6):1733-41

Svobodnik A, Yang P, Novotny PJ, et al. Quality of Life in 650 Lung Cancer Survivors 6 Months to 4 Years After Diagnosis. Mayo Clin Proc 2004; 79(8):1024-1030

Project 3 Health and Quality of Life of *Long-Term* Lung Cancer Survivors

The chance of surviving lung cancer beyond five years is approximately 15%. People who are alive five years after a lung cancer diagnosis have been regarded as long-term survivors. To date, published information is limited about the health status, health behavior, and QOL in long-term lung cancer survivors. We are studying lung cancer survivors to gain a better under-standing of the long-term disease outcome of these patients (including second cancers, survival time, and cause of death in deceased patients) and their health behaviors and QOL.

In an analysis of 148 long-term survivors who have returned our study questionnaire, 97% reported fairly good overall health. However, 16% indicated worsening health when compared to 1-year earlier.

- Approximately 50% of these survivors felt highly energetic.
- Thirty-three percent reported limited social engagement and 25% experienced emotional problems.
- Twenty percent were still working, 22% of whom reported handling a heavier workload compared to their same-age peers.
- Ninety percent reported eating fruit and/or vegetables daily, 58% were taking multivitamins, and 50% exercised regularly during the previous year.
- Seventy-three percent reported very good or best spiritual well-being.

Since lung cancer diagnosis, 83% reported no change in their family and social status, 12% were engaged, married, or partnered and 1% were divorced or separated.

Project 3 (continued)

Eighteen percent never smoked and 8% continued to smoke after diagnosis. Eighteen percent reported that their lung cancer had come back.

We concluded that most of the long-term lung cancer survivors had fairly good health overall, despite some reported physical, psychological, and social difficulties.

Yang P, Sugimura H, Ebbert JO, et al. Characteristics of Long-Term Lung Cancer Survivors. In: Department of Health and Human Services, National Cancer Institute, American Cancer Society, eds. Cancer Survivorship: Pathways to Health After Treatment. Washington, D.C., 2004; 51

Project 4 A Possible Lung Cancer Susceptibility Gene May be Identified Through a Collaborative Study

Mayo Clinic and 11 other research institutions and universities worked jointly to find the region in the human genome that harbors a lung cancer gene, and found it on a segment of chromosome 6. The researchers studied 52 families who had at least three first-degree relatives affected by lung, throat or laryngeal cancer.

What is the advantage of finding a lung cancer susceptibility gene? It could offer the greatest hope for screening for lung cancer. It could also explain why some people are at a higher risk for developing the disease even if they do not smoke and why smoking is especially deadly for those who do carry the gene. People carrying the lung cancer gene appear unusually sensitive to tobacco smoke. Even a small amount of smoking may be enough to cause lung cancer. This is in contrast to people who do not carry this gene, in whom the risk of lung cancer increases with the amount of cigarettes they smoked.

Doctors and researchers emphasized that the finding does not mean people should pay less attention to the dangers of cigarette smoking; instead, knowing this gene could assist doctors in finding people for whom exposure to tobacco smoke is particularly deadly.

Bailey-Wilson JE, Amos CI, Pinney SM, et al. A major lung cancer susceptibility locus maps to chromosome 6p23-25. Am J Hum Genet 2004; 75(3):460-474

Q&A Answers to questions frequently asked by participants in our study

Over the years, we have received many questions from people in our study about lung cancer and our research program. Here are answers to some of the most often asked questions:

Q "When should I expect to receive the findings from this research?" "Will I be notified of my blood test results and, if so, how long after I've had my blood drawn should I expect to hear something?"

A There are several goals of our research program that are represented by various projects. Some have produced findings (for example Projects 1 and 2), some only have early findings and are ongoing (for example Projects 3 and 4), and some are still enrolling patients.

Our study is one of the most useful for finding the gene(s) responsible for lung cancer because we are screening many people and studying a large number of genes. So far, a region on a chromosome, but not a lung cancer-specific gene has been found, as we described in Project 4. The main roadblock when trying to find such a gene(s) is getting enough lung cancer families with multiple living relatives willing to take part in and complete the study.

To protect the privacy and confidentiality of every person involved in our study, we do not link test results to individuals in our study. Therefore, our study findings are not retrievable for each patient. If any major lung cancer gene is found, we will let people in our study know by an update such as this communication.

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Q "Is adenocarcinoma of the lung a cancer of never-smokers?"

A The three major tumor subtypes of lung cancer are squamous cell carcinoma, adenocarcinoma, and small cell carcinoma; all subtypes are associated with tobacco smoke exposure. However, the influence of tobacco smoke on the risk of adenocarcinoma is not considered as great as that of the other two subtypes. This concept has been supported by reports that more never-smokers and fewer heavy smokers were observed in patients with adenocarcinoma than in those with squamous or small cell carcinomas. However, nearly all of the reports were from studies that compare people who have the disease with people who do not have the disease, and these studies generally had very few never-smokers available for analysis. Adenocarcinoma has been the most common subtype, particularly in women with primary lung cancer.

Using a prospective group of older women, we conducted an analysis of cigarette smoking and the three major subtypes of lung cancer. Two references are listed below. Our findings showed that, of the three major lung cancer subtypes, excess risk (ER, also called risk difference, measured by the difference of lung cancer risk between smokers and never-smokers) for heavy smokers compared to never- smokers was higher for adenocarcinoma (ER=206) than for squamous (ER=122) and small cell carcinomas (ER=104). Therefore, adenocarcinoma of the lung is more strongly associated with tobacco smoke exposure than previously recognized, supporting the opinion that tobacco smoke is much more powerful than any other exposures that may cause lung cancer.

Yang P, Cerhan JR, Vierkant RA, et al. Adenocarcinoma of the Lung is Strongly Associated with Cigarette Smoking: Further Evidence From a Prospective Study of Women. Am J Epidemiol 2002; 156(12):1114-1122

Ebbert JO, Yang P, Vachon CM, et al. Lung Cancer Risk Reduction After Smoking Cessation: Observations From a Prospective Cohort of Women. J Clin Oncol 2003; 21(5):921-926

Q "I've smoked marijuana; what do you know about that?"

A Marijuana seems to be well established as a social drug in Western countries, regardless of its current legal status. As with anything that is smoked, long-term smoking of marijuana could produce bronchitis. There are several case reports of young marijuana users with no history of tobacco smoking or other significant risk factors who were diagnosed with lung or other similar cancers. Several other case studies were suggestive of an association of marijuana smoking with head and neck cancers and oral lesions. In addition, several experimental and human studies suggest an association of marijuana use as a possible cause of cancers. Obviously, more studies are needed that focus on which factor is the real cause of the cancer and to distinguish the role of marijuana from those of other drugs and adverse environmental conditions. Your information regarding a history of smoking marijuana and other drugs will be helpful in future studies.

Q "I've already signed a consent form, so why do I need to sign this consent form?" "I've already donated blood, so why do I need to donate again?"

A We understand the inconvenience and sometimes redundancy patients go through when taking part in multiple studies. However, each study has specific goals. Each consent form defines the procedures to be done for that study. We hope you will consider our study. In order to minimize the inconvenience, we may ask your permission to use the blood sample that you donated in other studies whenever it is possible.

Comments and suggestions are welcome

Please feel free to contact our program coordinator, Sheila McNallan, at 507-266-1065 for additional information about this research program or to submit comments and suggestions.

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