Lung Cancer

The Importance of Early Detection

Lung cancer is the most common cancer worldwide, accounting for 1.2 million new cases annually and is the leading cause of cancer death in both men and women in the United States. Lung cancer has also increased in frequency over the last several decades. Several Eisenhower physicians came together to discuss the prevalence of the disease, its possible prevention and treatment options. Participants included a multidisciplinary group of board certified physicians, including Robert Johnson, MD, Radiation Oncology; Justin Thomas, MD, Interventional Pulmonology; Henry Tsai, MD, Medical Oncology; Davood Vafai, MD, Medical Oncology; and Joseph Wilson, MD, Cardiothoracic Surgery. Philip Shaver, MD, Cardiology, moderated the roundtable.

DR. SHAVER: Is it true that if we stop cigarette smoking, we entirely eliminate lung cancer?
DR. VAFAI: Absolutely not. About 15 percent of lung cancers are not related to tobacco or smoking, so even if you stop smoking or stop producing tobacco, there will still be lung cancers that are not related to tobacco. There's a lot of data coming out that radon is one of the major elements in risk factors of lung cancer. Cigarettes that are produced in the United States are designed to be addictive. They have radioactive compounds in them, and they have cyanide and arsenic in them. In addition to nicotine, there are many additives in cigarettes.

DR. SHAVER: We should discuss screening. To start, let's explain I-ELCAP and Eisenhower's role in it.
DR. VAFAI: I-ELCAP is a consortium of international institutions, both academic centers and community hospitals, and it stands for International Early Lung Cancer Action Project. Initially, it was primarily based in New York at Cornell, before expanding to become international. The program screens smokers.

DR. SHAVER: Is I-ELCAP examining secondhand smoke and its role in causing cancers? Does it have any importance at all?
DR. VAFAI: It certainly does. In I-ELCAP, we have a portion dedicated to secondhand smoke screening.

DR. SHAVER: I understand that there actually may be more pollutants or carcinogens in secondhand smoke, than even direct inhalation, but it gets dissipated over space fairly quickly. Dr. Tsai, can you describe what happens to the lining of the lung when it's exposed to carcinogens? For instance, you can remove a polyp and prevent colon cancer. What's the evolution of epithelium that these carcinogens do finally wind up in an invasive cancer?
DR. TSAI: The formation of cancer is often a progression of mutations. When you are exposed to carcinogens, there are different genetic defects leading to morphological changes, and multiple errors often compound into cancer formation. The lining of the airway can change from normal tissue to abnormal cancer tissue as a result of genetic defects.

DR. SHAVER: There are actually genetic or molecular changes in the cells that differentiate them from the normal cell lining.
DR. TSAI: Absolutely. There are some family histories where people are more susceptible to cancer formation. Scientists are looking at the genetic makeup of their genome that makes them moresusceptible to different kinds of cancerformations.

DR. SHAVER: If the people who have those weren't exposed to carcinogens, would theyget lung cancer?
DR. TSAI: It is less likely. It requires a combination of conditions coming together,genetics and environment. In general, healthy living is the best bet — never smoking, absolutely.

DR. SHAVER: There is certainly a reason to stop smoking. Smokers who quit for more than 15 years have an 80 to 90 percent reduction in their risk for lung cancer compared to those who continue to smoke. However, there is an increased risk of lungcancer for 30 to 40 years, even after quitting, and ex-smokers make up 50 percent of all new lung cancers. Therefore, screening becomes important. We have great examples of screening in PAP smears and colonoscopy. How successful is screening for lung cancer?
DR. VAFAI: Screening for lung cancer is the most productive and most effective of all the screenings, including prostate, breast and colon. When you consider the enormous mortality that is associated with lung cancer, this screening has much more impact on absolute number of deaths from lung cancer. For example, we have roughly 220,000 incidents of lung cancer a year in the United States. Out of these, 160,000 of these people die each year, so a 20 percent mortality reduction is 32,000 people a year. That is an enormous impact.

DR. SHAVER: At one time, the chest X-ray was thought to be a screening test. Of the screening tests available, where does the chest X-ray fall?
DR. THOMAS: There have been several large studies looking at chest X-rays, as well as chest X-rays with sputum analysis for screening for lung cancer. The studies had very disappointing results with no significant benefit as far as mortality in screenings with chest X-rays.

DR. SHAVER: The study comparing the chest X-ray to CT scanning showed CT scanning was far superior, correct?
DR. THOMAS: The National Lung Screening Trial looked at several thousand patients who were age 55 to 74, who smoked one pack a day for 30 years — 30 "pack years." In this particular trial, the patients had to have quit smoking within the last 15 years or continued to smoke during the trial period. The study compared chest X-rays to annual, low-dose CT scans. That's the study that Dr. Vafai was alluding to that showed a 20 percent reduction in mortality and also showed a reduction in all-cause mortality of about seven percent.

DR. SHAVER: Why not use a PET scan to screen these patients?
DR. JOHNSON: First and foremost, the initial reason is cost, but the second reason is even in the large CT versus chest X-ray studies, you still end up with a lot of false positives. The CT scan is fairly sensitive but not specific. PET scan is the same situation where you might end up requiring work-up for issues that aren't pertinent and can cause harm. Certainly, a PET scan gives a lot of information, but there are also resolution issues with PET/CT. Some of the really low grade, especially adenocarcinomas, what we used to call bronchoalveolar carcinomas, don't really light up on PET CT. And you don't get the same anatomic information from it that you do a proper diagnostic CT scan.

DR. SHAVER: Even with the imaging, you eventually need tissue to make the diagnosis of lung cancer. What is that process?
DR. VAFAI: This is a multidisciplinary decision where our team, which is composed of a pulmonologist, a radiologist and a medical oncologist, looks at the images and then decides what would be best — most of the time, that is a CT-guided biopsy. Under CT guidance, the radiologist will put a needle into the lung and get a biopsy.
DR. THOMAS: Each patient is individual and each particular circumstance may require a different type of modality to come to a diagnosis. Certainly the more peripheral lung lesions (the ones that are farther out near the edge of the lung) are optimal lesions for a CT-guided biopsy. Whereas, in situations where you have a single pulmonary nodule that is enlarging and there is no evidence for any lymph node involvement on a PET/CT scan, then a referral to a thoracic surgeon to remove the nodule is what's warranted. This way you can take it out and have a chance of cure at the same time. From a bronchoscopic perspective, there are methods in the works now, where we can guide our tools to the right spot and take biopsies. Eventually we may be able to treat it right then and there with radiofrequency ablation or other modalities that are coming down the pike. It is certainly a very exciting time for lung cancer diagnosis, staging and treatment.
DR. WILSON: I think Eisenhower is a leader in the field in this area. Once a month, there is a multidisciplinary lung cancer conference at Eisenhower Lucy Curci Cancer Center involving radiologists, pathologists, surgical oncologists, medical oncologists, radiation oncologists, pulmonary physicians, and referring doctors where we present

cases and in a multidisciplinary way, make a decision about what we would recommend for that patient — like the best way to obtain a biopsy to get the correct diagnosis. We help determine what stage cancer that patient may have, so we can lead them down the path of the appropriate choices for them, and the stages at which they should get that treatment.

DR. SHAVER: You really have to have expertise reading the CT scans. Not every hospital that has a CT scanner should be doing this kind of work.
DR. VAFAI: We've built up that expertise over the past 11 years. I think it's important that we differentiate our program from others — we have 11 years of experience with early detection of lung cancer with low-dose CT scans through I-ELCAP. We are nationally recognized as an experienced screening site by the Lung Cancer Alliance. Expertise in reading CT scans is only the beginning; our center offers comprehensive state-of-the-art diagnostics, surgical and if needed, oncology treatment of chest disease. Our multidisciplinary team of board certified physicians
who specialize in lung disease takes a collaborative approach when caring for patients.

DR. SHAVER: Lung cancer types include small cell, non-small cell, adenocarcinoma and squamous cell carcinoma. Adenocarcinomas and squamous cell are non-small cell cancers. It seems like the last several years, I've had more female patients who say they have never smoked and have lung cancer. It seems like adenocarcinoma is a greater frequency?
DR. VAFAI: That's correct. Women are more prone to develop lung cancer than men. So, they are more susceptible to develop cancer. In that, we include both adenocarcinoma and squamous cell.
DR. SHAVER: Why is that?
DR. VAFAI: Quite frankly, nobody really knows exactly why that's the case. But one reason is that more women are smoking.
DR. WILSON: In the United States, lung cancer deaths in women exceed breast cancer deaths, and in 2013, lung cancer deaths in European women surpassed breast cancer deaths, with lung cancer being the most deadly form of disease.
DR. TSAI: Before the EGFR [epidermal growth factor receptor] mutation was discovered, we noticed that Asian women who were never smokers had a tendency to get adenocarcinoma and they tended to have a better prognosis. We eventually found out they have a mutated EGFR pathway and that establishes a different subgroup of cancer population.

DR. SHAVER: When the multidisciplinary group meets to discuss patient cases, how do you approach the group of patients that make up about 15 percent of lung cancers who have a more aggressive tumor that even when you first diagnose it has usually spread? This is usually a small cell cancer in smokers.
DR. JOHNSON: It definitely changes the local therapy management, because it's thought to be a systemic disease at the time of diagnosis. These are cases, for instance, that Dr. Wilson is less likely to operate on, and even some of the radiation therapy techniques we use for early-stage non-small cell lung cancers, we would not use for early stage small cell lung cancers because it's really chemotherapy-based to deal with systemic disease, which is often microscopic at the time of diagnosis. You may think you just have one small lesion, but it's proven over time that just treating that locally is not enough in people with small cell lung cancer.

DR. SHAVER: Dr. Wilson, explain how your surgical work is influential to the entire treatment process.
DR. WILSON: I would say from a surgical standpoint, the most important thing is for us to know the appropriate stage of the cancer because cancer is spread not only via the blood stream to other places in the body, but it also spreads through lymphatics to the lymph nodes. Somewhere between 25 and 40 percent of patients have disease limited to the chest and those are patients for whom the most effective therapeutic modality is likely to be surgery. In 2011, 180,000 Americans were diagnosed with lung cancer, and of those, only 25 percent were eligible for surgical treatment as a primary therapy for lung cancer. Interestingly enough, only 29 percent of those were minimally invasive surgeries, which have become the main stay of surgical therapy now for lung cancer. There is a non-rib spreading key hole type incision, done either with what's called video-assisted thoracoscopy (or VATS) or a robotic approach. Those patients who have that type of procedure have less pain, they have fewer complications and they tend to go home sooner, but more importantly, patients can start their chemotherapy much, much sooner with a minimally invasive approach, because they heal faster. There is less of a delay in chemotherapy dose in patients who are healthier, so they are more likely to receive a full dose of chemotherapy than a reduced dose of chemotherapy. From a surgical standpoint, we play a valuable role in giving the oncologist the correct pathologic stage of the cancer after it's been removed, including the presence or absence of positive lymph nodes. The final decision regarding what treatment they receive after that can be made, whether it's chemotherapy or radiation therapy or cancer surveillance.

DR. SHAVER: Dr. Thomas, what can a pulmonologist do? For instance, if it's a bulky tumor in an airway, can you stent that airway?
DR. THOMAS: Absolutely. Interventional pulmonology is a fairly new field in medicine. Initial bronchoscopies were actually done with rigid bronchoscopes — which are hollow, long, metal tubes. Then the flexible bronchoscopes were invented and the rigid bronchoscope sort of fell out of favor because it required general anesthesia. There's been a renewed interest in rigid bronchoscopes recently with the advent of the interventional pulmonology field of medicine. With the rigid bronchoscopes, we can go in and [remove] tumors in the airway with multiple different modalities, such as laser therapy, cautery or cryotherapy and subsequently place a stent if there is external compression of the airways from large tumors. This is typically done as more of a palliative procedure in patients who are having significant symptoms of shortness of breath whose outlook in those situations is fairly poor. From a diagnostic standpoint, it is helpful to visualize the airways and see where that tumor is and perform biopsies for a diagnosis. Bronchoscopy, flexible or rigid, can help stage the tumor, both by visualizing the location of the tumor in the airways, and also by a modality called endobronchial ultrasound where we can identify enlarged lymph nodes in the chest and biopsy them to determine whether the cancer has spread to the lymph nodes. The nice thing about this is that it is a minimally invasive procedure that may actually save the patient from having an unnecessary surgery or more invasive procedure if it is found that the tumor involves the lymph nodes.

DR. SHAVER: Dr. Johnson, explain when radiation therapy is used.
DR. JOHNSON: Radiation therapy is used in patients who don't have metastatic disease. For small cell lung cancer, we use radiation therapy along with chemotherapy as a means to try to control both the local and systemic disease and there are cure rates reported to be in the 20 to 25 percent of patients in that particular group. Unfortunately, only 25 to 30 percent of patients with small cell lung cancer have localized disease, which unfortunately only makes up
25 to 30 percent of people diagnosed with small cell lung cancer to begin with. Most patients have more extensive disease when they're first diagnosed. Early-stage, when it's non-small cell lung cancer and a patient is eligible to have an operation, I absolutely encourage those patients to have surgery. It's much easier to follow those patients if they've had their tumor removed. In the circumstances of a patient who cannot have an operation, because of either tumor-related issues or just medical comorbidities, then we use stereotactic radiation therapy for early-stage tumors. We give anywhere between three and five treatments every other day, and it's a very large dose of radiation per treatment relative to how radiation is usually given. We are able to do that because we limit the size of tumor that we treat to something usually in the neighborhood of one to four centimeters in size. With this particular technique, we can control more than 90 percent of properly selected early-stage non-small cell lung cancers. Patients who have more advanced non-small cell lung cancers would have radiation therapy in a more protracted course, usually over about six or seven weeks of treatments, Monday through Friday, in an effort to try to control the disease
that we see in the chest. Unfortunately, the amount of radiation that you can give is limited by the tolerance of some of the important mediastinal structures and the lungs. Therefore, we can't use the same techniques we do for the smaller lung cancers, because side effects, especially esophagitis, are too severe. Unfortunately, outcomes are not as good for locally advanced non-small cell lung cancer. However, we do cure approximately 20 to 25 percent of these patients, which is similar to outcomes for small cell lung cancer.

DR. SHAVER: Where do you see treatment heading?
DR. VAFAI: The wave of the future is next generation sequencing. About 10 years ago, it cost more than $100,000 to do master gene sequencing of the entire tumor genome and identify novel pathways. Now, it costs around $2,000 to $3,000, which is very reasonable. We are now at the verge of identifying very, very important driver genes that we can target. I think the drive for the future in lung cancer will be next generation sequencing, to really identify where we need to target and what we need to target.
DR. TSAI: The buzz word in the cancer world is personalized medicine. Each person's cancer is different. In the oncology world, we try to do different things because the reality is cancer uses many ways to beat you. For instance, cancer builds new blood vessels, so we have entire anti-angiogenesis agents that block the ability of a tumor to seek and form new blood vessels. We find that cancer evades the immune system, and so currently there are a lot of exciting immune system-based vaccines and treatments for cancer. All of these things will come into play, and depending on what the person's genetic makeup is and what the tumor biology is,as Dr. Vafai noted, you can design a different, specifically tailored treatment to that particular person.

DR. SHAVER: Are you saying you're going to look at the patient's genome but also the cancer's genetics?
DR. TSAI: Certainly that would help. We need tumor genetics to see what is wrong with that tumor and how it evolves. Sometimes a metastatic lesion will have a different genetic makeup from a primary cancer lesion, so the more information you get, we can then design a better treatment plan.

DR. SHAVER: The U.S. Preventive Services Task Force (USPSTF) released their recommendation of annual screening for lung cancer using low-dose CT in adults aged 55 to 80 years old who have a "30 pack year" smoking history who currently smoke or have quit within the past 15 years. Under the Affordable Care Act, insurers are required by law to pay the entire cost of any screening service recommended by the USPSTF with a Grade A or B rating, without any copay or deductible.
DR. VAFAI: Low-dose CT lung cancer screening is definitely a cost-effective thing to do. Studies performed by Milliman, Inc., a leading international actuarial firm, as well as researchers at Legacy® Schroeder Institute for Tobacco Research and Policy Studies show strong evidence that early detection will significantly reduce lung cancer deaths — upwards of 70,000 a year and that low-dose CT scans are more cost-effective than commonly used screening methods for other cancers. The low-dose lung screening CT has proven to be a good test to detect lung cancer early when it is most treatable and research has shown that screening reduces death rates.