ACOSOG news:

Is wedge resection of early primary NSCLC sufficient?

by David Ota, MD, FACS, Durham, NC, and Heidi Nelson, MD, FACS, Rochester, MN

The standard surgical treatment for stage I lung cancer is lobectomy and mediastinal node dissection. However, it is not uncommon for a patient to be unable to tolerate such a procedure because of pulmonary risk factors.

Consider the example of a 73-year-old male patient with a 2.5 cm peripheral left upper lung nodule that was diagnosed as non-small cell lung carcinoma (NSCLC) by needle biopsy. There is no evidence of either mediastinal nodal or systemic disease by computed tomography (CT) and positron emission tomography scanning. You are concerned about the results of the pulmonary function tests. The forced expiratory volume (FEV1) is 45 percent and the CO_2 diffusion capacity (DLCO) is 40 percent. Your assessment is that this patient is a poor candidate for lobectomy and the radiation oncologist is very concerned that external beam radiation therapy (EBRT) will worsen his already compromised pulmonary function; furthermore, EBRT alone is unlikely to completely ablate the primary tumor. Wedge resection of the peripheral lung cancer is the only alternative but you have concerns about the adequacy of the tumor margins and local control of disease. Reports in the literature have shown a 20 percent recurrence rate.[1,2] Often the wedge resection staple line is adjacent to the primary tumor in order to preserve normal lung tissue. Thus, you consider if this is an adequate cancer procedure and if there is an alternative.

The development of radiation seeds (brachytherapy) has allowed the American College of Surgeons Oncology Group (ACOSOG) to design a clinical trial to answer these questions. ACOSOG has activated a phase III trial in which patients who have a <3 cm NSCLC and poor pulmonary function are eligible.

ACOSOG Z4032 is a randomized phase III trial of wedge resection versus wedge resection plus brachytherapy in high-risk patients. Primary endpoint is to ascertain whether patients treated by wedge resection plus brachytherapy have longer time to local recurrence as compared with the patients treated by wedge resection. Local recurrence includes recurrence within the same lobe or hilum (N1 nodes) or progression at the staple line after treatment effects such as scarring have subsided. The technique of placing brachytherapy seeds using mesh has been described in the literature.[3] There is minimum radiation exposure in the operating room.

The protocol defines high risk. The patient must meet at least one major criterion or meet a minimum of two minor criteria as described below:

Major criteria:

1. FEV1 ≤50 percent
2. DLCO ≤50 percent

Minor criteria:

1. Age ≥75 years
2. FEV1 51 percent to 60 percent predicted
3. DLCO 51 percent to 60 percent predicted
4. Pulmonary hypertension (defined as a pulmonary artery systolic pressure >40 mm Hg) as estimated by echocardiography or right heart catheterization)
5. Poor left ventricular function (defined as an ejection fraction of 40% or less)
6. Resting or exercise arterial pO_2 ≤55 mm Hg or SpO_2 ≤88 percent
7. pCO2 >45 mm Hg
8. Modified Medical Research Council (MMRC) dyspnea scale ≥3

In many ways, this trial design resembles the lumpectomy versus lumpectomy plus EBRT randomized trial for breast cancer conducted many years ago. Until the introduction of radiation seeds and lung stapling devices, it has not been possible to design such a trial for NSCLC until now. Another important

development is widespread use of CT scanning to screen for and detect early lung cancer. Just as mammography allows detection of nonpalpable disease for breast cancer, chest CT scanning is detecting lung cancer at early stage in those who are at high risk for developing this disease.

The accrual goal for Z4032 is 226 patients. This trial was recently activated and is accruing approximately five patients per month. A list of sites and investigators with Institutional Review Board (IRB) approval can be found at *http://www.clinicaltrials.gov*. Search for Z4032. Eligibility criteria are listed on this Web site.

If you have an eligible patient and do not have IRB approval at your hospital, please consider referring your patient to a nearby IRB-approved site listed on the Clinical Trials Web page. The number of IRB-approved sites is increasing and the list on the Web page is updated regularly.

ACOSOG is actively recruiting sites and if you are interested in participating in the trial, please contact LeeAnn Robinson at lee.a.robinson@duke.edu or call 919/668-8788. You may also go to *http://www.acosog.org* and obtain information about becoming a member and accessing the protocol.

Currently it is not clear if brachytherapy can reduce the local recurrence after wedge resection in these high-risk patients and through Z4032. ACOSOG is trying to answer this important clinical question via a prospective clinical trial. ACOSOG needs your help and involvement to accrue patients into this critically important trial.

References

1. Warren WH, Faber LP. Segmentectomy versus lobectomy in patients with stage I pulmonary carcinoma. *J Thorac Cardiovasc Surg*. 1994;107(4):1087-1094.
2. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1N0 non-small cell cancer by the Lung Cancer Study Group. *Ann Thorac Surg*. 1995;60(3):615-623.
3. Voynov G, Heron DE, Lin CJ, et al. Intraoperative ^{125}I Vicryl mesh brachytherapy after sublobar resection for high-risk stage I non-small cell lung cancer. *Brachytherapy*. 2005;4(4):278-285.

Disclosure: Dr. Ota has served on the Novartis Femara Surgical Advisory Board and is principal investigator of a Novartis grant for Z9001.

__Dr. Ota__ and __Dr. Nelson__ are ACOSOG Group Co-Chairs.

ACS Career Opportunities

The American College of Surgeons' online job bank

A unique interactive online recruitment tool provided by the American College of Surgeons.

An integrated network of dozens of the most prestigious health care associations.

Residents:

- View national, regional, and local job listings 24 hours a day, 7 days a week—free of charge.
- Post your resume, free of charge, where it will be visible to thousands of health care employers nationwide. You can post confidentially or openly—depending on your preference.
- Receive e-mail notification of new job postings.
- Track your current and past activity, with toll-free access to personal assistance.

Contact **phaar@facs.org** for more information.

health eCareers NETWORK