

Prevention of Acute COPD Exacerbations Is Critical

ARTICLES BY
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KEYSTONE, COLO. — Acute exacerbations of chronic obstructive pulmonary disease are a far more important driver of mortality than is generally appreciated.

Physicians often shrug off acute exacerbations of COPD as part of the natural course of the disease. Not so. There are several preventive therapies of proven efficacy, but to apply them most efficiently it's useful to turn to several large published studies that are instructive in identifying the high-risk subgroups, Dr. Barry Make said at a meeting on allergy and respiratory diseases.

"It's all about knowing how to prevent COPD exacerbations in the right COPD patient at the right time," emphasized Dr. Make, director of pulmonary rehabilitation at National Jewish Health and professor of medicine at the University of Colorado, Denver.

He was senior author of a large Veterans Affairs study that brought to light the serious consequences of acute exacerbations. The retrospective study involved 51,353 COPD patients discharged after a severe exacerbation, defined as one entailing hospitalization (*Chest* 2007;132:1748-55).

The key finding was that these patients had impressively high all-cause mortality: 21% over the subsequent year and 55% at 5 years. They also had COPD rehospitalization rates of 25% and 44% at 1 and 5 years, respective-

ly. The greater the number of prior COPD hospitalizations, the higher the subsequent all-cause mortality.

Median survival after index hospitalization was 4.2 years. Median length of stay during rehospitalization was 6.5 days. These hospitalizations are expensive. Acute exacerbations account for the bulk of health care expenditures for COPD, arguably the costliest of all the respiratory diseases, Dr. Make said at the meeting, which was sponsored by the National Jewish Medical and Research Center.

Frequent COPD exacerbations also are an enormous burden on patients' health-related quality of life. This was underscored in a classic study in which patients with three or more exacerbations over the course of a year had a mean 14.8-point worse score on the St. George's Respiratory Questionnaire than those with 0-2 exacerbations (*Am. J. Respir. Crit. Care Med.* 1998;157:1418-22).

The VA study demonstrated that patients who've had a COPD exacerbation are at increased risk for another. In another study, British investigators showed that these recurrent exacerbations are not random events over time, but rather they cluster such that the first 8 weeks after an initial exacerbation is a particularly high-risk period (*Am. J. Respir. Crit. Care Med.* 2009;179:369-74).

Dr. Make disclosed serving on advisory boards for Boehringer-Ingelheim, Glaxo-SmithKline, AstraZeneca, Dey, Forest, Novartis, Nycomed, and Schering-Plough. ■

How to Keep COPD Under Check

Preventing acute exacerbations is a top priority in patients with chronic obstructive pulmonary disease, and physicians can draw on three types of medication and one nonpharmacologic therapy of proven benefit for this purpose.

Each of the two drugs with Food and Drug Administration approval for the prevention of acute exacerbations is supported by a multiyear randomized trial of roughly 6,000 patients, which is unusually large for the field of COPD, Dr. Make noted.

Tiotropium (Spiriva, Boehringer-Ingelheim), a long-acting anticholinergic bronchodilator, received FDA approval for this indication last December.

In the massive 4-year Understanding Potential Long-Term Impacts on Function with Tiotropium (UPLIFT) trial, use of tiotropium resulted in a 14% reduction in the annual rate of moderate to severe exacerbations, compared with usual care (*N. Engl. J. Med.* 2008; 359:1543-54).

The other approved medication, fluticasone/salmeterol (Advair Diskus, GlaxoSmithKline), reduced moderate to severe exacerbations by 25% over 3 years in

the Towards a Revolution in COPD Health (TORCH) trial (*N. Engl. J. Med.* 2007;356:775-89).

Long-acting beta-agonists are also of proven efficacy in preventing acute exacerbations, as shown in a large meta-analysis that demonstrated a 21% reduction in relative risk (*JAMA* 2003;290:2301-12), but they are not FDA approved for this purpose, he said.

Pulmonary rehabilitation—a comprehensive program of education and physical exercise—is also of proven benefit in reducing acute exacerbations. A meta-analysis of six trials involving 230 patients demonstrated that pulmonary rehab reduced by 74% the relative risk of severe exacerbations entailing hospital admission (*Respir. Res.* 2005;6:54).

"For those patients who refuse to take medications, this is something else they can do." Pulmonary rehab, he stressed, is of value across the broad spectrum of COPD severity.

"I don't wait for patients to reach GOLD [Global Initiative for Chronic Obstructive Lung Disease] stage 3 or 4 to turn to pulmonary rehabilitation. ... I use this therapy in most of my patients," he said.

Novel Imaging Modality Investigates Pulmonary Nodules

KEYSTONE, COLO. — Management of a solitary pulmonary nodule 1 cm or less in size in a patient at intermediate risk for lung cancer remains an enormous challenge and considerable burden on the health care system.

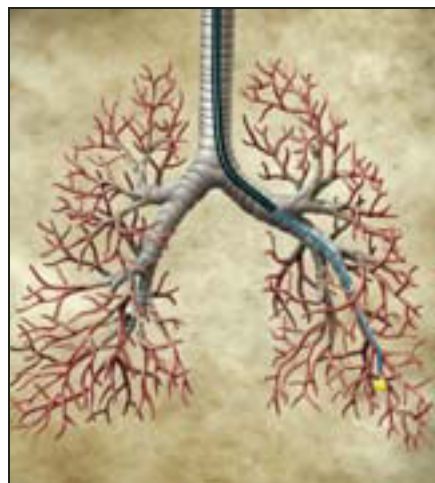
"This is where all the money is," Dr. Ali I. Musani observed at a meeting on allergy and respiratory diseases.

More than 150,000 patients per year in the United States present to physicians with a solitary pulmonary nodule (SPN). It's an incidental finding on 1 in 500 chest x-rays. The prevalence of an SPN on a screening CT in individuals at increased risk for lung cancer because of smoking history or occupational exposure is 13%.

In deciding what to do about these lesions, size matters.

"If a nodule is more than 1 cm and up to 2 cm, that's the ideal size for me, because that's where all my sampling technologies come into play. If a nodule is 1 cm or less, we still don't have very good technologies to biopsy them. If you start taking all these out, even in the high-risk population, the vast majority are going to be benign. So if they're worried, take it out; otherwise, follow by CT scan," said Dr. Musani, director of interventional pulmonology at National Jewish Health.

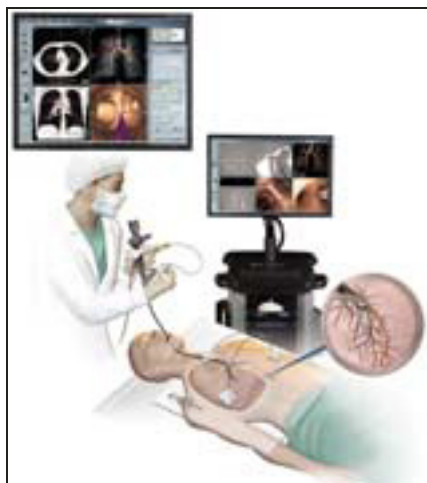
The standard recommendation for fol-



iLogic provides a three-dimensional road map for real-time navigation using a steerable endoscopic catheter guided by GPS-like technology.

low-up is 2 years of watchful waiting with CT every 6 months, looking for the lesion growth that would trigger a biopsy. When Dr. Musani is concerned about the possibility of bronchoalveolar carcinoma, however, that recommendation goes out the window.

"In recent years bronchoalveolar carcinoma has become very, very common. These cancers grow very slowly; 2 years of stability really means nothing. So if I see features of bronchoalveolar carcinoma on the CT, I don't care about the American College of Chest Physicians or American Thoracic Society recommen-



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dations, I keep doing CTs for 4 or 5 years," he said at the meeting, which was sponsored by the National Jewish Medical and Research Center.

A key problem is the lack of an established screening tool for lung cancer, despite the readily identifiable risk factors for the malignancy. More than three-quarters of lung cancers are diagnosed at stage III or IV, with a 5-year survival rate of only 15%. In contrast, lung cancers diagnosed at stage I have an 88% 10-year survival rate, so early diagnosis with the help of screening CT offers great hope.

CT is reliable for localizing and char-

acterizing a lung lesion, but a biopsy is still essential for diagnosis. A variety of tools is available for this purpose, including transthoracic needle aspiration (TTNA), standard bronchoscopy, sputum cytology, and surgical biopsy. Each has its disadvantages.

The most exciting diagnostic development of late is electromagnetic navigation bronchoscopy.

This proprietary technology, marketed by superDimension Inc., utilizes a \$20,000 software package to convert a high-resolution CT into a three-dimensional road map for real-time navigation using a steerable endoscopic catheter guided by GPS-like technology while the patient lies in an electromagnetic field. This provides minimally invasive access to SPNs located deep in the lungs, well beyond the reach of standard bronchoscopy. Once at the target, biopsy needles and forceps are passed through the catheter channel.

Dr. Musani's personal experience with the superDimension i-Logic electronic navigation bronchoscopy system has been quite favorable.

"I want to see data on 1- to 2-cm lesions. That's the real challenge," the pulmonologist noted.

Dr. Musani disclosed serving on the speakers bureaus for Cardinal Health, Olympus, and superDimension. ■