VOL. 5 • NO. 11 • NOVEMBER 2010

CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

COURTESY CHARLES MANLEY

Low-priority patients who received lung transplants lived a median of 4 years; low-priority patients who did not receive transplants survived for a median of nearly 5 years, Dr. Mark J. Russo said.

Lung Transplants May Cut Life Span in Some

BY ROBERT FINN
Elsevier Global Medical News

OJAI, CALIF. – About 90% of potential lung transplant recipients have lung allocation scores less than 40. Although this puts them in the lowest priority category, they receive about 90% of the available organs. Now a new study appears to show that the life expectancy of these low-priority recipients is actually shorter if they receive a transplant than if they remain on the waiting list.

Dr. Mark J. Russo and his colleagues from Columbia University in New York used patient-level data from the United Network for Organ Sharing in a study of all 6,082 lung transplant candidates older than the age of 12 years who were placed on the transplant list in the United States between May 2005 and May 2009.

The investigators determined that those low-priority recipients lived a median of 4 years after transplant, compared with low-priority patients who did not receive a transplant and survived for a median of nearly 5 years. Thus, a transplant resulted in a net decrease in life expectancy of nearly a year for these patients.

The current system of lung allocation scores (LAS) began in 2005, replacing a priority ranking that was based entirely upon the patient's length of time on the waiting list. The LAS is calculated on the basis of medical urgency and expected posttransplant survival. For purposes of the LAS, urgency carries a greater weight than does expected survival.

In presenting these data at the annual meeting of the Western Thoracic Surgical Association, Dr. Russo noted that patients with moderate priority scores (LAS 50-79) tended to reap the greatest survival benefit from their lung transplants. Patients in that group lived a median of 3-4 years if they received a transplant. On the other hand, patients in that group who did not receive a transplant lived a median of well less than 1 year,

See **Lung Transplants** • *page 14*

Screening With CT Linked to Drop in Lung Cancer Death

NCI unveils long-awaited trial data.

BY PATRICE WENDLING
Elsevier Global Medical News

A large randomized national trial has provided the first evidence of a significant reduction in lung cancer deaths with a screening test.

The National Lung Screening Trial (NLST) reported a 20.3% reduction in lung cancer mortality among heavy smokers screened with low-dose helical computed tomography (CT), as compared with those given standard chest x-rays. The trial enrolled more than 53,000 older, high-risk individuals.

In addition, deaths from any cause, including lung cancer, were 7% lower among participants screened with low-dose helical CT, also known as spiral CT.

The initial results were released today by the study sponsor, the National Cancer Institute, after the study's independent data and safety monitoring board recommended halting the trial.

"The fact that low-dose helical CT provides a decided benefit is a result that will have implications for screening and management of lung cancer for many years to come," Dr. Christine Berg, project officer for the lung screening study at the NCI, said in a statement.

Beginning in 2002, the NLST recruited about 53,500 American men and women, aged 55-74 years, who were current or former smokers with a smoking history of at least 30 pack-years. It randomly assigned them to receive three annual screens with low-dose helical CT or chest x-ray. Helical CT uses x-rays to obtain a multiple-image scan of the entire chest during a 7- to 15-second

See **Screening** • *page 9*

INSIDE

Reaching Kids With Asthma at School

BY PATRICE WENDLING
Elsevier Global Medical News

VANCOUVER, B.C. – A school-based intervention that focused on medication adherence and reducing exposure to tobacco smoke significantly improved outcomes in inner-city children with asthma in a randomized trial.

Children receiving the school-based intervention had almost 1 additional symptom-free day per 2-week period during the peak winter asthma season of November to February.

The number of symptom-free days increased from an average of 8 days for all children at baseline to 11.9 days per 2-week period with the intervention vs. 11.2 days with usual care.

"This difference is larger than what has been seen with more intensive and costly interventions," said Maria Fagnano, M.P.H., of the University of Rochester (N.Y.) Medical Center.

The children receiving the intervention were significantly more likely than controls to

See **Asthma** • *page 2*

CHEST Physician
60 Columbia Rd.,
Bldg. B, 2nd flr.
Morristown, NJ 07960

CHANGE SERVICE REQUESTED

Presorted Standard
U.S. Postage
PAID
Permit No. 384
Lebanon Jct. KY

School-Based Therapy Effective

Asthma • *from page 1*

have fewer nights with symptoms (mean 1.5 nights vs. 2.0 nights), fewer days with limited activity (1.2 vs. 1.6), and fewer days with rescue medication use (1.59 vs. 2.61), Ms. Fagnano reported at the annual meeting of the Pediatric Academic Societies.

The intervention group also was significantly less likely than controls to have any acute visit for asthma (12% vs. 18%). In addition, the intervention group had fewer days absent from school due to asthma (0.3 days vs. 0.4 days).

Although additional efforts are needed to evaluate costs of the intervention and to develop dissemination strategies, collaborations with schools provide a unique opportunity to reach high-risk children and target those at greatest need for assistance, said Ms. Fagnano.

"This type of intervention is widely applicable for asthma care in the community nationwide, as well as for management of other chronic diseases, and could potentially reduce disparities between poor and nonpoor children," she said.

The School-Based Asthma Therapy (SBAT) trial, led by colleague Dr. Jill Halterman, was implemented in 2006 in 54 schools and preschools in Rochester, N.Y., to reduce morbidity in poor children aged 3-10 years with physician-diagnosed asthma.

The school nurse was given a canister of preventive medication (fluticasone propionate or fluticasone propionate with salmeterol), with a spacer and mask as appropriate, and asked to give one dose of medication to the child during the school day. A supply of preventive asthma medications also was delivered to parents, who were instructed to use the medications on days the child did not attend school.

To ensure appropriate dosing, the researchers conducted follow-up interviews after the first 3 months, with adjustments made according to national guidelines for children who continued to have persistent symptoms.

The intervention also used motivational interviewing to counsel the primary caregiver about how to reduce environmental tobacco smoke (ETS) in the home for smoke-exposed children, Ms. Fagnano said. Overall, 54% of children lived with one or more smokers at baseline. A home-based counseling session was delivered by a trained nurse, with two follow-up telephone calls made at 1 and 3 months after the 30-minute session.

In the usual care group, parents and physicians were notified of the child's asthma severity and encouraged to initiate appropriate preventive treatments, but no medication was provided, she said.

At baseline, 69% of children were on preventive medications, 73% received Medicaid, 58% were male, 63% were black, and 28% were Hispanic. Their mean age was 7 years.

There were 265 children in each arm of the study.

In a regression analysis, the intervention was associated with 0.92 days per 2 weeks more symptom-free days (*P* less than .001), Ms. Fagnano said.

A stratified analysis showed a significant intervention effect on the primary outcome of symptom-free days for children with and without ETS exposure in the home. The mean number of symptom-free days among non-ETS exposed children was 11.6 days in the treatment group vs. 10.9 days in the control group; and was 11.6 days vs. 10.0 days, respectively, in smoke-exposed children, she said.

COLLABORATIONS WITH SCHOOLS PROVIDE A UNIQUE OPPORTUNITY TO REACH HIGH-RISK CHILDREN AND TARGET THOSE WITH GREATEST NEED.

An audience member remarked on the dramatic improvement observed even among controls. Ms. Fagnano said that monthly phone calls for follow-up assessment could have "clued parents in to what the child was experiencing," and that asthma calendars given to these families also may have helped them notice more symptoms.

Another audience member expressed admiration for the overall outcomes, but questioned how they can be sustained during the summer, when children leave school.

Ms. Fagnano said that children with asthma traditionally do better in the summer, but she agreed that sustainability is a concern and that a supplemental summer educational program may be needed.

The School-Based Asthma Therapy trial was supported by grants from the National Heart, Lung, and Blood Institute, as well as grants from the Halcyon Hill Foundation.

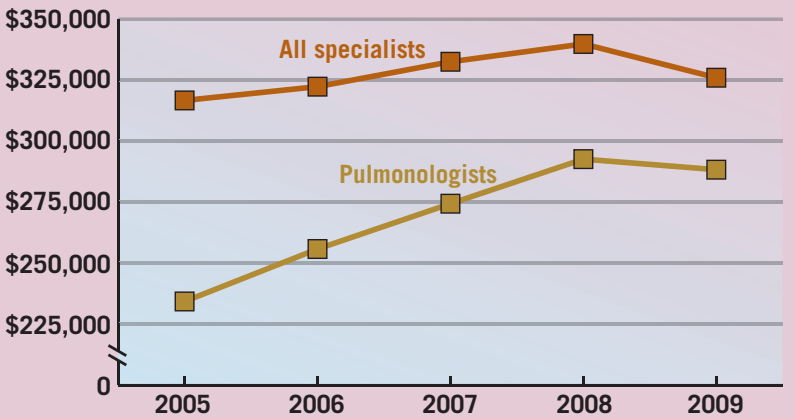
Ms. Fagnano and Dr. Halterman disclosed no financial conflicts related to the study. ■

IN THIS ISSUE

CHEST PHYSICIAN Is Online
CHEST PHYSICIAN is available on the Web at www.chestnet.org/accp/chest-physician.

DATA WATCH

Pulmonologists' Median Income Fell 1.5% in 2009



Note: 2009 figure from annual survey based on data for 245 pulmonologists in 116 group practices.
Source: Medical Group Management Association

Elsevier Global Medical News

AMERICAN COLLEGE OF CHEST PHYSICIANS®

AMERICAN COLLEGE OF CHEST PHYSICIANS
Editor in Chief Paul A. Selecky, M.D., FCCP
Deputy Editor W. Michael Alberts, MD, FCCP
President David D. Gutterman, MD, FCCP
Executive Vice President and CEO Paul A. Markowski, CAE
Senior Vice President, Communications Stephen J. Welch
Manager, Editorial Resources Pamela L. Goorsky
Medical Copy Editor II Peggy E. Perona, R.D.
Section Editors
Marilyn G. Foreman, M.D., FCCP - **Pulmonary Perspectives Editor**
Loren J. Harris, M.D., FCCP - **Pulmonary Perspectives Deputy Editor**
Neil Halpern, M.D., FCCP - **Critical Care Commentary**
James Parish, M.D., FCCP - **Sleep Strategies**

EDITORIAL ADVISORY BOARD
W. Michael Alberts, M.D., FCCP, Florida
Joseph Barney, M.D., FCCP, Alabama
Jun Chiong, M.D., FCCP, California
Stephen Field, M.D., FCCP, Calgary
Richard Fischel, M.D., FCCP, California
Nicola A. Hanania, M.D., FCCP, Texas
Carl Kaplan, M.D., FCCP, Missouri
Burt Lesnick, M.D., FCCP, Georgia
Philip Marcus, M.D., MPH, FCCP, New York
Mark L. Metersky, M.D., FCCP, Connecticut
Jeana O'Brien, M.D., FCCP, Texas
Nirupam Singh, M.D., California

E-mail: chestphysiciannews@chestnet.org

CHEST PHYSICIAN

CHEST PHYSICIAN, the newspaper of the American College of Chest Physicians, provides cutting-edge reports from clinical meetings, FDA coverage, clinical trial results, expert commentary, and reporting on the business and politics of chest medicine. Each issue also provides material exclusive to the members of the American College of Chest Physicians. Content for **CHEST PHYSICIAN** is provided by International Medical News Group and Elsevier Global Medical News. Content for NEWS FROM THE COLLEGE is provided by the American College of Chest Physicians.
The statements and opinions expressed in **CHEST PHYSICIAN** do not necessarily reflect those of the American College of Chest Physicians, or of its officers, regents, members, and employees, or those of the Publisher. The American College of Chest Physicians, its officers, regents, members, and employees, and Elsevier Inc. do not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to products, drugs, or services mentioned herein.

Address Changes: Fax changes of address (with old mailing label) to 973-290-8245.

POSTMASTER: Send change of address (with old mailing label) to CHEST PHYSICIAN, 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960.

CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Elsevier Inc., 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250.

ELSEVIER SOCIETY NEWS GROUP, A DIVISION OF INTERNATIONAL MEDICAL NEWS GROUP

President, IMNG Alan J. Imhoff
Director, ESNG Mark Branca
Editor in Chief Mary Jo M. Dales
Executive Editors Denise Fulton, Kathy Scarbeck
Managing Editor Leanne Sullivan

Circulation Analyst Barbara Cavallaro, 973-290-8253, b.cavallaro@elsevier.com
Executive Director, Operations Jim Chicca
Director, Production and Manufacturing Yvonne Evans
Production Manager Judi Sheffer
Creative Director Louise A. Koenig
Display Advertising Manager The Walchli Tauber Group: 443-512-8899, fax 443-512-8909, greg.pessagno@wt-group.com

ADVERTISING OFFICES 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250
CLASSIFIED ADVERTISING OFFICES The Walchli Tauber Group, 2225 Old Emmorton Rd., Suite 201, Bel Air, MD 21015, 443-512-8899
EDITORIAL OFFICES 5635 Fishers Lane, Suite 6000, Rockville, MD 20852, 240-221-4500, fax 240-221-2541

Cardiopulmonary Exercise Testing Underutilized

BY MITCHEL L. ZOLER
Elsevier Global Medical News

Cardiopulmonary exercise testing "offers the clinician the ability to obtain a wealth of information beyond the standard exercise ECG testing" but is underused and underappreciated today, a panel of experts said in a clinician's guide and scientific statement by the American Heart Association.

Cardiopulmonary exercise testing (CPX), "when appropriately applied and interpreted, can assist in the management of complex cardiovascular and pulmonary disease," wrote the group of 15 experts assembled by the American Heart Association's Exercise, Cardiac Rehabilitation, and Prevention Committee (Circulation 2010 [doi:10.1161/CIR.0b013e3181e52e69]).

"CPX is more informative than standard ECG testing in the diagnostic assessment of unexplained dyspnea and skeletal muscle myopathy and prognostic assessment of heart failure patients. It is [also] useful in evaluating disability in patients with cardiovascular disease and pulmonary disease," said Dr. Gary J. Balady, professor of medicine at Boston University and chair of the panel that wrote the new guide for CPX in adults. CPX also has proved reliable for assessing stroke patients with gait impairments.

"The consensus of the writing group is that CPX is underused, as its utility is not widely understood. We hope that our paper stimulates interest in and use of the test," Dr. Balady said in an interview.

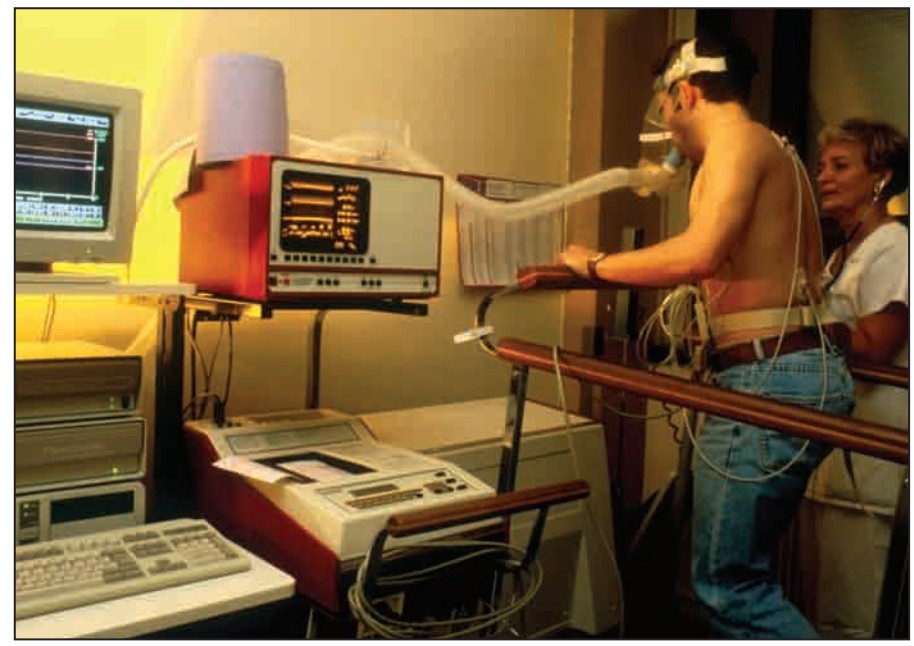
The recommendations by the panel derived mostly from published data even though no randomized trial has directly addressed the diagnostic and prognostic applications of CPX.

"Perhaps the document will stimulate research in this area," said Dr. Balady, who is also director of preventive cardiology and the noninvasive cardiovascular laboratory at Boston Medical Center.

CPX systems use rapidly responding sensors whose readings translate into measurements of oxygen uptake and carbon dioxide output of a patient at rest, during exercise, and during recovery. In the United States, the preferred exercise method is a treadmill.

CPX measures a series of variables including maximal aerobic capacity, ventilatory threshold, peak respiratory exchange ratio, and pulmonary function testing.

Cardiopulmonary exercise testing also integrates standard measures from an ECG exercise stress test with gas exchange assessment, producing a more comprehensive patient evaluation.



©B.S.I.P./Custom Medical Stock Photo Inc.

Emerging applications of cardiopulmonary exercise testing include assessment of pulmonary resection patients and of patients with pulmonary hypertension.

Standard exercise ECG data collected include heart rate, heart rate recovery, heart rhythms, ECG changes, blood pressure, and symptoms such as dyspnea and chest discomfort.

Additional emerging applications of CPX include assessment of adults with congenital heart disease, patients who have undergone pulmonary resection or bariatric surgery, and those with pulmonary hypertension, ischemic heart disease, a cardiac pacemaker, or arrhythmias.

"More studies are needed to assess the increasing number of variables that can be derived from CPX as well as their utility in many conditions that affect the cardiovascular and pulmonary systems," the guide said.

Most academic medical centers and hospitals with transplant programs have CPX available, Dr. Balady said.

"Unless a physician has a specialty practice with large numbers of patients with the conditions" for which CPX has proven utility, "it would be best to refer the patient to a specialty center," he noted.

Medicare reimbursement for both the technical and physician components of a CPX test runs about $250.

Physicians who train to perform CPX must first be certified in exercise testing. CPX training is typically available from companies that manufacture and market CPX systems or at centers that perform CPX.

Although no CPX training standards exist, a reasonable criterion is that the operator should have supervised and interpreted 50 CPX examinations during training, Dr. Balady said.

Dr. Balady and the other members of the panel that wrote the CPX guide said that they had no relevant conflicts of interest. ■

COMMENTARY

Dr. Jun R. Chiong, MPH, FACC, FCCP, comments: With regard to exercise training, the HF-ACTION Trial (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) has been published and included 2,331 patients at 82 study sites throughout the United States, Canada, and France. The participants were randomized to receive usual care or to receive usual care plus an exercise training program that began under supervision but then transitioned to home-based, self-monitored workouts.

Stress Test Agent Can Be Used in Asthma, COPD Patients

BY RICHARD M. KIRKNER
Elsevier Global Medical News

PHILADELPHIA – Individuals with asthma or chronic obstructive pulmonary disease can tolerate the imaging agent regadenoson well if they need to undergo cardiac stress testing, a study has shown.

Dr. Bruce Prenner, a San Diego allergist, reported on findings from a multicenter trial involving 999 patients who received either regadenoson or a placebo.

"Regadenoson has a greater affinity for the A2B receptors and the other types of receptors, and thus the risk of bronchospasm and bronchoreactive events should be quite low," he said at the annual scientific session of the American Society of Nuclear Cardiology.

The risks of adenosine inducing breathing problems in individuals with asthma and COPD have been well documented. This study set out to determine how regadenoson affected forced expiratory volume in 1 second (FEV_1) in 999 study subjects, 532 with asthma and 467 with COPD.

About half of the patients received the placebo. The primary end point was a greater than 15% decrease in forced expiratory function from baseline within 2 hours of the dose being administered, Dr. Prenner said.

In the asthma group, 1.1% of patients in the regadenoson arm had an FEV_1 decrease greater than 15%, compared with 2.9% of patients in the placebo group, he said. Among patients with COPD, 4.2% receiving regadenoson and 5.4% on placebo met the primary end point, he said.

Respiratory problems such as wheezing, dyspnea, obstructive airways disorder, and tachypnea were more common in the patients on regadenoson than in those on placebo: 13% vs. 2%, respectively, in the asthma group; and 19% vs. 4% in the COPD patients.

"The asthma patients had less frequency in terms of previous studies," Dr. Prenner said.

The variation between regadenoson and placebo was driven by dyspnea, a known side effect of A2A agonists, he noted.

However, within 1 day of injection, the use of short-acting bronchodilators was similar for those who received both regadenoson and placebo, Dr. Prenner reported.

In subjects with asthma, 1.4% of the regadenoson group and 1.1% of the placebo group used the inhalers. Among patients with COPD, the rates of inhaler use were 1.6% and 1.3%, respectively, for the regadenoson and placebo cohorts.

REGADENOSON'S AFFINITY FOR THE A2B RECEPTORS AND THE OTHER RECEPTORS SHOULD MAKE THE RISK OF BRONCHOSPASM LOW.

The investigation showed no clinically meaningful differences between treatments in pulmonary function tests in either group, according to Dr. Prenner. Although the incidence of adverse events was higher in patients taking regadenoson, the adverse event profile was similar to that reported in previous regadenoson trials that had been conducted in nonasthmatic COPD patients. Of six serious adverse events with regadenoson, three were considered treatment related, Dr. Prenner added.

"This information should be very useful in considering the selection of regadenoson as a bottom-line stress agent for myocardial perfusion imaging in these types of patient populations," Dr. Prenner said.

Dr. Prenner is a scientific adviser to Astellas, which is the manufacturer of regadenoson, and serves on its speakers bureau. ■

Endobronchial Valves Improve Emphysema Modestly

BY MARY ANN MOON
Elsevier Global Medical News

Unilateral lobar treatment with endobronchial valves produces modest improvements in lung function, exercise tolerance, and symptoms in patients with advanced, heterogeneous, hyperinflated emphysema, according to a report in the New England Journal of Medicine.

However, these benefits come with substantial costs in the months after implantation: more frequent exacerbations of chronic obstructive pulmonary disease (COPD), pneumonia distal to the valves in more than 4% of cases, hemoptysis related to oozing from granulation tissue, and pneumothorax, said Dr. Frank C. Sciurba of the University of Pittsburgh and his associates.

They assessed the safety and efficacy of endobronchial valves, compared with standard medical care, in what they described as the first randomized, prospective, multicenter study of the devices, the Endobronchial Valve for Emphysema Palliation Trial (VENT).

The study involved 321 patients (aged 40-75 years) who were randomly assigned to receive either the unidirectional valves (220 subjects), which block regional inflation while allowing exhalation, or standard medical therapy (101 controls).

The valves are designed to reduce the volume (hyperinflation) of the most severely damaged lobe, allowing expansion of the more viable adjacent lobe.

A mean of 3.8 valves was placed in each patient via bronchoscopy. The valves were placed in only one lung (in the lobar, segmental, or subsegmental bronchi, depending on the patient's anatomy) to completely isolate the targeted lobe. Moderate sedation was used in 71% of patients and general anesthesia in 29%. The mean duration of the procedure was 34 minutes.

The composite efficacy end point was the percent change in forced expiratory volume in 1 second (FEV_1) and distance achieved in the 6-minute walk test at the 6-month follow-up. The primary safety end point was a composite of six major complications arising within 6 months: death, empyema, massive hemoptysis, pneumonia distal to the valves, pneumothorax or air leak of more than 7 days' duration, or ventilator-dependent respiratory failure of more than 24 hours' duration.

Quality of life, exercise capacity, dyspnea, and daily oxygen use also were assessed as secondary end points.

At 6 months, FEV_1 increased by 4.3% in the valve group and decreased by 2.5% in control group, for a mean between-group difference of 6.8%. Similarly, distance traveled in the 6-minute walk test increased by 2.5% in the valve group and decreased by 3.2% in the control group, for a mean between-group difference of 5.8%, Dr. Sciurba and his colleagues reported (N. Engl. J. Med. 2010;363:1233-44).

Patients who received the valves also showed modest changes in all secondary end points.

However, the 6-month rate of composite complications was 6.1% in the valve group, compared with 1.2% in the control group. This included six deaths in the valve group and none in the control group. At 1 year, the complication rates were 10.3% and 4.6%, respectively.

The most common adverse event related to valve placement was pneumonia distal to the valve, which developed in 4.2% of patients within 1 year of the procedure. Hemoptysis that required bronchoscopic inspection was significantly more common in the valve group (approximately 12%) than in controls (0%). Similarly, pneumothorax developed more often in the valve group (5.2%) than in controls (2.4%), as did COPD exacerbations requiring hospitalization (7.9% and 1.1%, respectively).

"In 12 months of follow-up, valves were removed in 31 patients for reasons including retrieval of a migrated valve (in 8 patients), the patient's request for an unspecified reason (in 7), pneumonia management (in 3), COPD exacerbations (in 2), hemoptysis (in 1), and other reasons (in 7)," the researchers wrote. In addition, further bronchoscopies were required in 23% of the valve group, compared with only 1% of the control group.

After the trial was completed in 2007, another eight patients underwent elective removal of the valves because of adverse events, and three others experienced spontaneous expectoration of a valve, the investigators said.

The VENT study was funded by Emphasys Medical (now Pulmonx) and a grant to Dr. Sciurba from the National Institutes of Health. Dr. Sciurba and several associates reported ties to numerous drug and device manufacturers. ■

COMMENTARY

Dr. Nicola Hanania, FCCP, comments: Lung volume reduction surgery has been shown to improve outcomes in a subgroup of patients with emphysema. However, this intervention may be associated with increased risk of perioperative complications. Several endoscopic modalities to achieve lung volume reduction are currently being evaluated. The report above summarizes important results from one of these studies that evaluated one of two valves being evaluated in patients with emphysema. While none of these valves is currently approved by the FDA for patient use, the results of the study suggest that this valve may be beneficial in some but not all patients. However, the risk of adverse effects in this trial is not minor and should be taken into consideration in evaluating such an intervention. Nevertheless, this is one of only a few large studies that evaluated the efficacy and safety of a nonsurgical and a nonpharmacologic intervention in the management of hyperinflation in patients with emphysema, and thus its results cannot be ignored.

Benchmarks Did Not Predict Lung Cancer Surgery Deaths

BY ROBERT FINN
Elsevier Global Medical News

OJAI, CALIF. – In a prospective study of 778 patients undergoing surgery for non–small cell lung cancer, investigators found no significant relationships between any of 53 health care benchmarks and mortality.

The investigators did, however, find an association between 10 critical benchmarks and morbidity, said Dr. Robert J. Cerfolio at the annual meeting of the Western Thoracic Surgical Association.

"It appears that the quality of the patient is a better predictor of outcomes than … the quality of the health care provider," said Dr. Cerfolio of the University of Alabama at Birmingham. Dr. Cerfolio conducted the study along with Dr. Ayesha S. Bryant, also from the university.

In performing the study, the investigators first developed a list of 53 facets of optimal patient care that might be expected to affect outcomes in patients undergoing surgery for non–small cell lung cancer (NSCLC).

They identified 14 preoperative benchmarks, 8 day-of-surgery benchmarks, 18 intraoperative benchmarks, and 13 postoperative benchmarks. Within those, they designated 10 "critical" benchmarks – those that appeared necessary for a good outcome.

Among the critical benchmarks were enrolling the patient in a cardiopulmonary rehab program at home prior to surgery, performing the lobectomy in less than 100 minutes, losing less than 125 mL of blood during the operation, and discharge by postoperative day 4.

The 778 patients ranged in age from 19 to 86 years and received their operations between 2007 and 2009. Physicians performed a lobectomy or bi-lobectomy on 64% of the patients, sublobar resection on 34%, and pneumonectomy on 2%. Among the patients, 15% had diabetes mellitus, 21% had coronary artery disease, and 35% had a smoking history of at least 20 pack-years.

The health care team met 99.8% of the day-of-surgery benchmarks, 96.8% of the intraoperative benchmarks, 94% of the postoperative benchmarks, and 90.5% of the preoperative benchmarks. Of the critical benchmarks, 89% of the patients received all 10 and 98% got 9 of the 10.

But only 60% of the patients received all 53 of the benchmarks, a result that Dr. Cerfolio described as disappointing and embarrassing.

About 2% of the patients died, 9.25% experienced major morbidity, and the overall morbidity rate was 27%.

In a univariate analysis the investigators identified six patient characteristics associated with mortality, including an age above 67 years, the type of resection, and forced expiratory volume in 1 second (FEV_1) greater than 78%. But in a multivariate analysis that controlled for numerous potential confounders, only two factors remain statistically significant: whether the patient was a smoker and whether he or she had coronary artery disease.

The quality of the patient appears to predict outcomes better than the quality of the health care provider.

DR. CERFOLIO

The researchers identified 11 different factors with a univariate relationship to major morbidity, but the only ones that were statistically significant in the multivariate analysis were age, smoking status, coronary artery disease, and whether the health care team delivered all 10 critical benchmarks.

Similarly, 11 factors had a significant univariate relationship with overall mortality, but only 4 of them remained statistically significant in the multivariate analysis. They were age greater than 67, smoking status, type of pulmonary resection, and meeting all 10 critical benchmarks.

Dr. Cerfolio noted some limitations of this study. For one thing, the investigators developed the 53 benchmarks subjectively, and some of the benchmarks were nothing more than surrogates for good outcomes, such as "avoid ICU admission," or "go home by postoperative day 4." In addition, the study was relatively small, and it was conducted at a single institution.

Dr. Cerfolio said that he undertook the study in part to evaluate whether "pay-for-performance" seemed to be appropriate in treating patients requiring surgery for NSCLC. "In this very small study the concept of pay for performance is unsupported," he concluded.

Dr. Cerfolio serves as a consultant for Deknatel, Closure Medical, and Neomend, and as a speaker for E Plus Healthcare, Medela, Ethicon, Covidien, OSI Systems, Precision Medical, and DaVinci Medical Group. ■

Pages 4a—4f

Algorithm Matches NSCLC Treatments to Biomarkers

BY SHERRY BOSCHERT
Elsevier Global Medical News

SAN FRANCISCO – Five biomarkers that were identified in molecular studies can predict the likelihood of a patient's response to specific chemotherapeutic drugs for non–small cell lung cancer, according to Dr. Gerold Bepler, president of the Karmanos Cancer Institute at Wayne State University in Detroit.

To help clinicians use these biomarkers to choose individualized treatments for new patients, he has proposed an algorithm based on the data collected thus far. Dr. Bepler cited the following studies in his talk at the meeting, which was sponsored by the American Association for Cancer Research.

The Evidence

In a subgroup analysis of a chemotherapy trial for patients with pulmonary adenocarcinoma, 261 patients with EGFR-1 (epidermal growth factor receptor–1) mutations had significantly longer progression-free survival if they were treated with gefitinib (Iressa) rather than a carboplatin-paclitaxel combination. The opposite was true for 176 patients who tested negative for EGFR mutation (N. Engl. J. Med. 2009;361:947-57).

Several studies have shown that high levels of DNA ERCC1 (excision-repair cross-complementation group 1) protein in NSCLC tumors predicted longer survival in patients who were randomized to treatment without chemotherapy, as well as a lower likelihood of response to platinum-containing chemotherapy, when these patients were compared with those who didn't have high levels of ERCC1.

One study, a phase III community-based trial by Dr. Bepler and his associates, also showed that higher levels of the enzyme RRM1 (the regulatory subunit of ribonucleotide reductase) predicted poor response to chemotherapy containing gemcitabine (Gemzar), compared with patients who have low levels of RRM1 (J. Clin. Oncol. 2009;27:5808-15).

"The higher the RRM1 expression, the less likely the tumor will shrink from gemcitabine-containing therapy," Dr. Bepler said.

Another recently identified mutation – a rearrangement between the EML4 and ALK genes – occurs in about 5% of lung cancer patients. Six forms of this gene fusion have been seen so far, and preliminary, unpublished data suggest that its presence predicts better 1-year survival regardless of treatment, as well as a 64% response rate to chemotherapy using the experimental agent crizotinib, according to Dr. Bepler. "That is a stunning number," he said. "I'm quite sure that one can safely say that this is a predictive marker of efficacy with this drug."

Expression of thymidylate synthase (TS) protein in NSCLC tumors also predicted better outcomes regardless of treatment, as well as better response to neoadjuvant chemotherapy using pemetrexed (Alimta) in preliminary studies, he added.

The Algorithm

Based on these data, Dr. Bepler proposed that oncologists who see a new patient with advanced NSCLC first conduct an EGFR mutation analysis. "If there is a mutation, the patient unequivocally should be a candidate for an EGFR-tyrosine kinase inhibitor," he said.

If there is no response or if the mutation is not present, assess the tumor for EML4/ALK rearrangement. If present, treat with crizotinib.

If there's no response or no sign of EML4/ALK fusion, assess the tumor for ERCC1 and RRM1 and treat patients who have low levels with a platinum plus gemcitabine combination.

If there's no response, assess levels of ERCC1 and TS. Treat patients with low ERCC1 and TS levels with a platinum plus pemetrexed combination.

For the approximately one-fourth of patients who fail all these treatments or who have high levels of ERCC1, treat with a "default regimen" of a taxane plus a nonplatinum drug, Dr. Bepler advised.

Dr. Bepler has been a consultant for Genzyme, owns an interest in Genmab and Eli Lilly, and has received research funding from Eli Lilly and Sanofi-Aventis. ■

COMMENTARY

Dr. W. Michael Alberts, FCCP, comments: Using data gleaned from recent separate but related studies, Dr. Gerold Bepler has proposed a potentially useful treatment algorithm for non–small cell lung cancer. Designing individualized treatment regimens based on biomarkers is theoretically appealing. One hopes that it will prove to be clinically beneficial.

observed in an additional 22 patients 12 to 17 years of age who were treated with DULERA in another clinical trial. The safety and efficacy of DULERA have not been established in children less than 12 years of age.

Controlled clinical studies have shown that inhaled corticosteroids may cause a reduction in growth velocity in pediatric patients. In these studies, the mean reduction in growth velocity was approximately 1 cm per year (range 0.3 to 1.8 per year) and appears to depend upon dose and duration of exposure. This effect was observed in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with orally inhaled corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with orally inhaled corticosteroids has not been adequately studied.

The growth of children and adolescents receiving orally inhaled corticosteroids, including DULERA, should be monitored routinely (e.g., via stadiometry). If a child or adolescent on any corticosteroid appears to have growth suppression, the possibility that he/she is particularly sensitive to this effect should be considered. The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the risks associated with alternative therapies. To minimize the systemic effects of orally inhaled corticosteroids, including DULERA, each patient should be titrated to his/her lowest effective dose *[see Dosage and Administration (2.2)]*.

8.5 Geriatric Use

A total of 77 patients 65 years of age and older (of which 11 were 75 years and older) have been treated with DULERA in 3 clinical trials up to 52 weeks in duration. Similar efficacy and safety results were observed in an additional 28 patients 65 years of age and older who were treated with DULERA in another clinical trial. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. As with other products containing $beta_2$-agonists, special caution should be observed when using DULERA in geriatric patients who have concomitant cardiovascular disease that could be adversely affected by $beta_2$-agonists. Based on available data for DULERA or its active components, no adjustment of dosage of DULERA in geriatric patients is warranted.

8.6 Hepatic Impairment

Concentrations of mometasone furoate appear to increase with severity of hepatic impairment *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

10.1 Signs and Symptoms

DULERA: DULERA contains both mometasone furoate and formoterol fumarate; therefore, the risks associated with overdosage for the individual components described below apply to DULERA.

Mometasone Furoate: Chronic overdosage may result in signs/symptoms of hypercorticism *[see Warnings and Precautions (5.7)]*. Single oral doses up to 8000 mcg of mometasone furoate have been studied on human volunteers with no adverse reactions reported.

Formoterol Fumarate: The expected signs and symptoms with overdosage of formoterol are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the following signs and symptoms: angina, hypertension or hypotension, tachycardia, with rates up to 200 beats/min., arrhythmias, nervousness, headache, tremor, seizures, muscle cramps, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, hypokalemia, hyperglycemia, and insomnia. Metabolic acidosis may also occur. Cardiac arrest and even death may be associated with an overdose of formoterol.

The minimum acute lethal inhalation dose of formoterol fumarate in rats is 156 mg/kg (approximately 63,000 times the MRHD on a mcg/m^2 basis). The median lethal oral doses in Chinese hamsters, rats, and mice provide even higher multiples of the MRHD.

10.2 Treatment

DULERA: Treatment of overdosage consists of discontinuation of DULERA together with institution of appropriate symptomatic and/or supportive therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of DULERA. Cardiac monitoring is recommended in cases of overdosage.

Manufactured by 3M Health Care Ltd.,
Loughborough, United Kingdom.
Manufactured for Schering Corporation, a subsidiary of

MERCK & CO., INC.
Whitehouse Station, NJ 08889 USA.

6/10 **32704107T-JBS**

Cyclophosphamide Is of Most Benefit for Worst SSc-ILD

BY M. ALEXANDER OTTO
Elsevier Global Medical News

MARINA DEL REY, CALIF. – Cyclophosphamide is most likely to help scleroderma interstitial lung disease patients early in the course of their disease if they have extensive lung fibrosis, high Rodnan skin scores, and documented declines in forced vital capacity, according to findings from an unpublished subgroup analysis presented by Dr. Philip Clements, professor of medicine at the University of California, Los Angeles.

The news comes from ongoing analysis of the Scleroderma Lung Study, and is soon to be published, Dr. Clements said at a rheumatology seminar sponsored by the school.

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: Patients with fibrosis associated with collagen vascular disease have been reported to have better response rates to treatment than those with idiopathic fibrosis. This benefit was also suggested in an early Scleroderma Lung Study report of cyclophosphamide use (improvement in FVC of 4.16% between groups); however, the improvement failed to sustain at 24 months. With continued follow-up, the researchers have identified a cohort with thicker skin and increased radiographic involvement who may respond better. Given the nature of this disease, continued research, follow-up, and assessment of newer agents (mycophenolate) appears justified.

Dr. Clements was a lead investigator in the randomized, controlled clinical trial, which compared a 12-month course of cyclophosphamide treatment given to 79 patients with systemic sclerosis interstitial lung disease (SSc-ILD) against placebo given to 79.

At 18 months' follow-up, the cyclophosphamide-treated patients improved slightly over baseline forced vital capacity (FVC), whereas patients in the placebo group declined. The treatment difference between the two groups was 4.16% in favor of the cyclophosphamide patients (Am. J. Respir. Crit. Care Med. 2007;176:1026-34).

The treatment differences "collapsed at 24 months, unfortunately," Dr. Clements said.

However, in subsequent analysis, a subset of patients were identified who responded better to treatment: those with Rodnan skin thickness scores greater than 24 and fibrosis involving more than 50% of a lower-lung field.

Radiologists assessed the extent of lung fibrosis in the subjects by visually inspecting high-resolution thoracic CT images.

A software program has been developed to do the scoring, and should be available to clinicians within 3 years, Dr. Clements said.

For the subset of the treated group that responded better to cyclophosphamide, FVC at 18 months was 73% of predicted values for healthy, age-matched controls, but it was 63% of predicted values in the placebo group, although the treatment differences again collapsed at 24 months.

Even so, "the more fibrosis at baseline, the more likely [patients] are to respond," Dr. Clements said. "Thick skin suggests their lungs are likely to respond to cyclophosphamide," he noted.

Additional analysis is planned to assess the clinical relevance of the findings, he said.

Patients from the Scleroderma Lung Study, which ran in 2000-2004, have been followed for an average of 8 years. So far, "cancer and death have not been associated with cyclophosphamide therapy," Dr. Clements said.

Given the results, he said he treats SSc-ILD patients with cyclophosphamide if they have mild to moderate restrictive lung disease and are within 7 years of scleroderma diagnosis.

They must also have FVCs that are lower than 80% of predicted values, along with fibrosis involving 25% or more of any lung field accompanied by ground-glass opacifications and dyspnea involving difficulty in climbing two or three flights of stairs.

With those patients, "my treatment approach is similar to that of the National Institutes of Health's lupus nephritis protocol," Dr. Clements said. The protocol includes the following:

- Pulse cyclophosphamide IV (500-750 mg/m^2 per month (assuming normal renal function) for 6-12 months.
- Repeat pulmonary function tests every 3 months while patient is on cyclophosphamide.
- Upon completion of the infusion, switch to long-term mycophenolate mofetil (2-3 g/day orally).

Azathioprine (3-5 mg/kg per day) is an option if mycophenolate mofetil cannot be tolerated.

Mycophenolate mofetil is the subject of Scleroderma Lung Study II, which will compare a 2-year course of the drug in SSc-ILD patients against a 1-year course of cyclophosphamide, followed by placebo.

Mycophenolate mofetil "looks promising," Dr. Clements said, based on several small, observational studies.

About 30 patients have enrolled in the trial since November 2009. "We need 150," he said.

Information on the trial can be accessed on the Web at http://sls.med.ucla.edu. The trial is also listed on clinicaltrials.gov.

Dr. Clements disclosed that he is a member of Gilead Sciences' pulmonary hypertension advisory board. ■

Systemic Sclerosis Is Fatal for Half of Patients

Independent predictors of death included proteinuria, pulmonary arterial hypertension.

BY HEIDI SPLETE
Elsevier Global Medical News

Patients with systemic sclerosis have about a 55% chance of dying from their disease. Specifically, more than half of systemic sclerosis deaths are caused by pulmonary fibrosis, pulmonary arterial hypertension, and heart-related problems that are attributable to the disease, according to an analysis of data from an international registry.

The overall mortality from systemic sclerosis (SSc) remains high, wrote Dr. Anthony J. Tyndall of the rheumatology department at the University of Basel (Switzerland) and his colleagues.

In order to identify the causes and predictors of death in SSc patients, the researchers conducted a review of data from 5,860 adults who were enrolled in the European League Against Rheumatism Scleroderma Trial and Research group (EUSTAR) database between 2004 and 2008.

A total of 284 deaths were reported in the database during the period of the study. Of these, complete data were available for 234 deaths via questionnaires completed by the medical centers that reported a death in an SSc patient (Ann. Rheum. Dis. 2010;69:1809-15).

The investigators determined that more than half (55%) of the deaths were directly attributable to SSc. Another 41% of deaths were not related to SSc, and the cause of death was not known in the remaining 4%.

Pulmonary fibrosis was the most common cause of death among the SSc deaths (19%), followed by pulmonary arterial hypertension (14%) and myocardial causes (14%). Most myocardial causes were attributed to arrhythmia.

Another 4% of the SSc deaths were caused by renal crises.

These findings contrast with data from other autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis, in which clinically overt myocardial infarctions are more common causes of death, the researchers noted.

The main causes of death that were not related to SSc were infections (33%), malignancies (31%), and cardiovascular diseases (29%). However, 25% of the patients who died of non-SSc causes had SSc-related comorbidities that likely contributed to their deaths, the researchers noted. These comorbidities included pneumonia, sepsis, and gastrointestinal hemorrhage. If these cases were added to the deaths directly caused by SSc, "the disease-related death toll would be as high as 65%," according to the researchers.

The average age of patients entering the study was 57 years, and 80% were women.

After controlling for multiple variables, Dr. Tyndall and his colleagues determined that the independent predictors of death in SSc patients included proteinuria, pulmonary arterial hypertension (PAH), forced vital capacity (FVC) less than 80% of normal, shortness of breath on exertion, reduced diffusing capacity of the lung for carbon monoxide (DLCO), and older age at onset of SSc (defined by the first signs of Raynaud's phenomenon and modified Rodnan skin scores).

Sex was not an independent predictor of death in this study, but the researchers said that the effect of sex can be accounted for by the other variables.

The study was limited by possible biases in the coding of death certificates, but the findings support data from previous studies showing PAH and pulmonary restriction as independent risk factors for mortality in SSc patients, the researchers noted.

"The EUSTAR figures presented here are useful in estimating the number of patients that need to be included in clinical trials that investigate survival as an end point," they said.

EUSTAR exists under the auspices of the EULAR Standing Committee for Clinical Affairs and is funded by a research grant from EULAR. The researchers had no financial conflicts to disclose. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: The report from the EUSTAR database provides information regarding mortality causes in patients with systemic sclerosis. Of the mortality directly attributed to SSc, pulmonary fibrosis and pulmonary arterial hypertension were significant contributors. Although potentially useful for guiding research, it is difficult to make more definitive conclusions from this summary beyond what is currently known.

Lungs Show Effects From Sept. 11

BY MARY ANN MOON
Elsevier Global Medical News

Rescue workers' impairment of lung function after the Sept. 11, 2001, terrorist attack on the World Trade Center did not recover substantially during the subsequent 6 years, according to a report in the New England Journal of Medicine.

Values of forced expiratory volume in 1 second (FEV_1), which showed large declines after both immediate and months-long exposures to dust from the collapse of the World Trade Center (WTC), never rebounded as they did in many studies of rescue workers exposed to other chemical, woodland, and urban fires, said Dr. Thomas K. Aldrich of Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, N.Y., and his associates.

They assessed long-term pulmonary effects in 12,781 firefighters and emergency medical services (EMS) workers who had spirometry testing at routine occupational health assessments both before and after the Sept. 11 attack and who worked at the WTC site in the weeks afterward. Lung function was assessed through 2008.

As noted in previous studies, FEV_1 values, adjusted for subjects' race, age, height, weight, and sex, were significantly lower than normal at 6 months and 1 year after Sept. 11.

Unexpectedly, there was no evidence of recovery of lung function for the next 6 years. Among workers who had never smoked, the average decline was 592 mL for firefighters and 504 mL for EMS workers, the authors said (N. Engl. J. Med. 2010;362:1263-72).

"Before 9/11, few firefighters had abnormal results on spirometry (below the lower limit of the normal range), and almost none had values that were significantly abnormal clinically (less than 70% of the predicted value). After Sept. 11, there were immediate increases in both frequencies, with subsequent stabilization at approximately 13% of firefighters who had an FEV_1 value below the lower limit of the normal range and 2% who had measurements under 70% of the predicted value," the authors noted.

The corresponding numbers for EMS workers were 11.0% with a below-normal FEV_1 value and 2.5% who had an FEV_1 below 70% of the predicted value. After 9/11, those percentages more than doubled and remained elevated at 23.0% and 7.5%, respectively, among EMS workers in 2008.

The study was supported by the National Institute for Occupational Safety and Health and the National Institutes of Health. Dr. Aldrich had no relevant conflicts of interest. ■

Progress Seen in Lowering CLABSI Rate

BY DIANA MAHONEY
Elsevier Global Medical News

The overall number of central line–associated bloodstream infections during the first half of 2009 in states with legislative mandates to report such infections was 18% lower than predicted based on national estimates from the previous 3 years.

That finding emerged from a health care–associated infections (HAIs) summary report issued by the Centers for Disease Control and Prevention and described in a media telebriefing.

The report includes overall national data on central line–associated bloodstream infections (CLABSIs) and, for the first time, state-specific data from health care facilities in states that mandate CLABSI reporting to the CDC's National Healthcare Safety Network, according to Dr. Don Wright, deputy assistant secretary for healthcare quality in the Department of Health and Human Services' Office of Public Health and Science.

The report also compares national and state data from January to June 2009 with national data from 2006-2008 using standardized infection ratio (SIR) calculations, which were adjusted for patient mix by type and bed size and hospital affiliation with a medical school.

The report is a "benchmark for progress" on the goals of the HHS Action Plan to Prevent Healthcare-Associated Infections, HHS Secretary Kathleen Sebelius said in a statement. "On a state level, this report can serve as a baseline from which we can assess the impact of state-based HAI prevention programs, including those funded by the 2009 American Reinvestment and Recovery Act," she added.

According to the report, in the 17 states that, as of June 30, 2009, had mandated the reporting of CLABSIs to their state health departments, 1,538 health care facilities reported 4,615 CLABSIs from January to June 2009 – nearly 1,000 fewer than the 5,619 that were predicted.

Eleven of the 17 states had an SIR significantly less than the nominal value 1.0 (representing the number of expected infections), while only two had SIRs that were significantly higher than 1.0, said Dr. Arjun Srinivasan, associate director for the CDC's Healthcare-Associated Infection Prevention Program. In nearly all of the states with mandated reporting, at least 25% of health care facilities reported no CLABSIs, the report noted.

Although the initial results are encouraging and represent early progress in the comprehensive strategy to reduce, prevent, and ultimately eliminate HAIs outlined in the HHS Action Plan, the current report "is only the first step," Dr. Srinivasan said, noting that the "real tests" will be every 6 months, with the release of updated reports that allow comparisons of state-specific progress over time.

"The report provides a snapshot of where the country stands on efforts to prevent [CLABSIs] and tells us how we are performing nationally against prevention goals outlined in the action plan," Dr. Srinivasan said. More importantly, however, "it will serve as a baseline from which states can assess their own progress," he said, noting that the baseline statistics should not be used to compare states with each other, but rather to determine "whether our prevention efforts are driving [infection] numbers down."

The 18% national reduction observed thus far reflects a broader implementation of infection control guidelines, enhanced tracking and measurement, and the combined efforts of clinicians, state health departments, federal agencies, professional organizations, and consumer advocates to enhance prevention efforts, "but more still has to be done" to meet the goal of a 50% reduction by 2013 outlined in the action plan, he said.

The Association for Professionals in Infection Control and Epidemiology (APIC) said in a statement that it was encouraged by the report's findings. "While not all healthcare-associated infections are preventable, APIC believes that every healthcare institution should be working toward a goal of HAI elimination. Many of our member facilities have seen that central line–associated bloodstream infections can be reduced to zero, and that in many instances 'zero' can be maintained." ■

The full CDC report is available at www.cdc.gov/hai/statesummary.html.

Patients at High Risk for Postop Sepsis Identified

BY MARY ANN MOON
Elsevier Global Medical News

The rates of sepsis and septic shock following general surgery are so excessive that identifying high-risk patients and screening them at 12-hour intervals for signs and symptoms may be warranted.

An analysis of data on more than 360,000 general surgery patients showed that those at highest risk are older than 60 years of age, undergo emergency rather than elective surgery, and have a major comorbidity. The findings suggest that patients with any of these three risk factors "warrant a high index of suspicion [and] would most likely benefit from mandatory sepsis screening," said Dr. Laura J. Moore and her associates at Methodist Hospital, Houston.

To date, programs to limit perioperative complications have focused on thromboembolism, surgery-related MI, and surgical site infections. These efforts have produced a significant decline in all three complications and in related mortality.

But the incidences of postoperative sepsis and septic shock have remained alarmingly high – far greater than those of thromboembolism and MI – and the associated mortality also remains excessively high (50%), the investigators noted.

To characterize the severity and extent of postoperative sepsis and septic shock, Dr. Moore and her colleagues analyzed information that had been collected prospectively in the American College of Surgeons NSQIP (National Surgical Quality Improvement Program) database. They examined data on 363,897 patients treated at 121 academic and community hospitals in 2005-2007.

A total of 8,350 patients (2.3%) developed sepsis, and 5,977 (1.6%) developed septic shock following general surgery. In comparison, pulmonary embolism developed in 0.3% and MI in 0.2%.

The development of sepsis raised the rate of 30-day mortality 4-fold, whereas septic shock raised it 33-fold, they said (Arch. Surg. 2010;145:695-700).

"Septic shock occurs 10 times more frequently than MI and has the same mortality rate; thus, it kills 10 times more people," they said. "Therefore, our level of vigilance in identifying sepsis and septic shock needs to mimic, if not surpass, our vigilance for identifying MI and PE."

Because closer monitoring of all surgical patients for signs and symptoms of sepsis is not realistic, it should be limited to those at highest risk. In this analysis, the percentage of patients older than age 60 was only 40% in the overall study group, compared with 52% in the group that developed sepsis and 70% in the group that developed septic shock.

The rate of sepsis was only 2% and that of septic shock was only 1% in patients undergoing elective procedures, compared with rates of approximately 5% for both sepsis and septic shock in patients undergoing emergency procedures.

Finally, about 90% of patients who developed sepsis and 97% of those who developed septic shock had at least one major comorbidity, compared with 70% of those who did not develop sepsis. "The presence of any of the NSQIP-documented comorbidities increased the odds of developing sepsis or septic shock by sixfold" and raised the 30-day mortality by 22-fold, Dr. Moore and her associates said.

Clinicians at Methodist did not always identify sepsis in the most timely way. The hospital implemented a program in which patients with any of these risk factors were screened every 12 hours for heart rate, white blood cell count, temperature, and respiratory rate. The program lowered sepsis-related mortality.

This study was supported by the Methodist Hospital Research Institute. No disclosures were reported. ■

More Detailed Results to Come

Screening • *from page 1*

breath-hold, whereas a standard chest x-ray produces only a single image of the chest from a sub-second breath-hold.

At the time of the Oct. 20, 2010 analysis, 354 deaths from lung cancer had occurred in the CT arm vs. 442 in the chest x-ray group. Approximately 25% of deaths in the NLST were due to lung cancer.

NCI director Dr. Harold E. Varmus said the well-designed study used rigorous scientific methods and that its findings could spare countless lives.

"Lung cancer is the leading cause of cancer mortality in the U.S. and throughout the world, so a validated approach that can reduce lung cancer mortality by even 20% has the potential to spare very significant numbers of people from the ravages of this disease," he said. "But these findings should in no way distract us from continued effort to curtail the use of tobacco, which will remain the major causative factor for lung cancer and several other diseases."

Like other screening strategies, the use of low-dose helical CT has disadvantages, including the cumulative effects of radiation from multiple CT scans, complications among patients who need additional testing to make a definitive lung cancer diagnosis, and the anxiety and added cost associated with investigating incidental findings picked up on CT.

[Editor's note: In 2009, investigators reported that low-dose CT screening was associated with twice the rate of false positives and more unneeded interventions, compared with chest x-ray, in a randomized feasibility trial that preceded the NLST. But low-dose CT also detected twice as many lung cancers as did chest x-ray screens in that study.]

Although the NLST trial cohort was ethnically representative of the high-risk U.S. population, the researchers noted that participants were highly motivated and screened at major medical centers. Thus, the results may not accurately predict the effect of CT screening for other populations.

"What has happened here is that the technology shows you can cut down on lung cancer deaths, the leading cause of cancer mortality, and save nearly as many lives as the number of people who die from breast cancer per year. We as a medical community now need to figure out how to do this in a way that the cost is acceptable to the public," Dr. Bruce E. Johnson, an official with the American Society of Clinical Oncology and director of the Lowe Center for Thoracic Oncology at the Dana-Farber Cancer Institute in Boston, said in a statement.

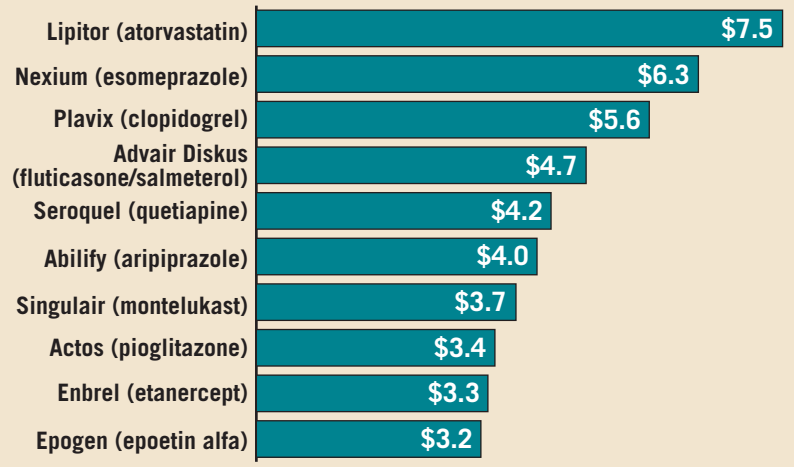
'WE AS A MEDICAL COMMUNITY NOW NEED TO FIGURE OUT HOW TO DO THIS IN A WAY THAT THE COST IS ACCEPTABLE TO THE PUBLIC.'

A more detailed analysis of the NLST results is expected to be published in the coming months, although a paper describing its design and protocol was published by the journal Radiology and is available at http://radiology.rsna.org/cgi/content/abstract/radiol.10091808. More information can be viewed online at www.cancer.gov/clinicaltrials/noteworthy-trials/nlst.

The trial was conducted at 33 sites by the American College of Radiology Imaging Network and the Lung Screening Study group. The study was sponsored by the National Cancer Institute. ■

DATA WATCH

Advair Diskus Fourth in U.S. Pharmaceutical Sales in 2009
(in billions)



Source: IMS Health

ELSEVIER GLOBAL MEDICAL NEWS

PRESIDENT'S REPORT

My Term as ACCP President: A Year in Review

I am most honored to have served as the 72nd President of the ACCP. As the year comes to a close, I want to review our accomplishments. I considered my charge to not only continue the excellent work that transpires but also to shepherd the transition as we welcomed a new EVP/CEO, Paul A. Markowski, CAE. We took this opportunity to look at "where we were, where we are, and where we want to be" in order to plan the next phase of College activities.

Organizational Changes

The Environmental Snapshot: With the change of volunteer and staff leadership, we began taking stock of all facets of the ACCP to determine where and how we could progress as an organization. An environmental snapshot of all the areas of operation were taken and presented to the leadership in January 2010.

DR KALPALATHA K. GUNTUPALLI, FCCP

Strategic Planning: Our strategic planning began with the environmental snapshot that resulted in the ACCP Strategic Plan 2010–2011, which set ambitious goals that looked several years ahead and delineated strategies and metrics for measuring success in achieving these goals.

Restructuring – April 2010: ACCP office staff was restructured to meet work flow.

Reassessing the Real Estate Needs/Space Needs – August 2010: We are revisiting the space and real estate needs of the College with the help of CB Richard Ellis. The findings will be deliberated by the Board.

Reevaluating Government and Advocacy Needs – September 2010: Major changes in the medical practice environment, as a result of the recently enacted health system reform legislation, will require the ACCP to be versatile, nimble, and strategic in its advocacy. Thus, we are developing new models to shape of our future advocacy efforts. A task force was created to assess the needs, direction, and alignment of resources to accomplish the task, led by then President-Elect David Gutterman, MD, FCCP.

Bylaws and Policy Manuals: As part of the periodic review process, a task force, led by then President-Designate Suhail Raoff, MBBS, FCCP, and Bylaws Committee Chair, John Buckley, MD, FCCP, is reviewing the bylaws and the policy/procedure manuals. With the help of the general counsel for the College, we hope to wrap this up shortly.

Transparent Leadership: To increase transparency, a dashboard with access to financial information, a month-to-month running list of projects' status, and access to minutes has been put into place. This transparency in leadership/administration is achieved by the ability to look up information as it related to the strategic vision.

Improved Communication: A monthly leadership e-newsletter was launched in August 2010 to ensure the 500 plus committee members and other leadership are aware of ongoing issues/projects.

Conflict of Interest Policy Revisited: A task force (Ian Nathanson, MD, FCCP – Chair) has reviewed, revised, and developed tiered policies for the ACCP leadership. This is to be presented for adoption after input from the leadership at the CHEST 2010 Board of Regents meeting.

Publications: *CHEST*

We leveraged technology to deliver our education content globally. The College launched the ACCP Board Review e-books on the *CHEST* journal platform to create the www.chestpubs.org site and the first ACCP iPhone®/iPad™/iPod® touch app for ACCP-SEEK. This summer, *CHEST* reached its highest impact factor (6.36) and ranking (3rd of 43 respiratory journals) in its 75-year history.

Strategic Networking

Critical Care Societies Collaborative (CCSC): The CCSC represents the four major critical care professional and scientific societies (AACN, ACCP, ATS, and SCCM). This year, we hosted a CCSC retreat to move forward on a series of joint projects, among them a joint US Department of Health and Human Services/CCSC National Awards Program for Achievements in Prevention of Hospital-Acquired Infections.

Critical Care Research Agenda: Another joint project was the development of a critical care research agenda. The work product of the task force on the CCSC research agenda hopefully will serve as a valuable road map to both investigators and funding agencies.

Role of Clinical Research Results in the Practice of Critical Care Medicine: The ACCP, ATS, and SCCM have come together through a task force to deliberate on this topic. The product of this group, "The Role of Clinical Research Results in the Practice of Critical Care Medicine," will help guide bedside clinicians to interpret the data resulting from clinical research in critical care.

Telemedicine Research Conference: A multicenter survey of tele-ICU interventions was performed by the ACCP Critical Care Institute. As a result of this, the Agency for Healthcare Research and Quality funded a conference to come up with a consensus statement on the research agenda for ICU telemedicine. This conference was held in Northbrook at the ACCP, in March 2010. Planned as a project of the CCSC, this interdisciplinary group includes representatives from the four CCSC organizations and users/experts of tele-ICUs around the country. The primary product of the conference is a multisociety consensus statement on the research agenda in ICU telemedicine that will be published in peer-reviewed literature, disseminated to key stakeholders in critical care delivery and health-care system design, and used to inform potential future requests for applications/proposals.

ACCP faculty and friends at Anzhen Hospital (Beijing) Conference/Exhibit, April 2010.

Forum of International Respiratory Societies (FIRS): My overarching "theme" as ACCP President was to extend our reach to the international community. As luck would have it, I served as President during 2010: The Year of the Lung (YOL), a global initiative instituted by FIRS, a collaboration of the world's leading professional respiratory organizations, including the ACCP. YOL advocated for lung health globally to reduce lung disease morbidity and mortality. The ACCP took the lead in antitobacco education, lung cancer awareness, COPD programs for primary care, the ACCP Capitol Hill Caucus (March 2010), World Spirometry Day, and many other events.

On the Domestic Front

I aspired to make the ACCP the "one stop shop" for the education, practice management, performance improvement/monitoring, and advocacy needs of the membership. Through our strategic planning process, we acknowledged that our core competency – providing the best clinical education in chest medicine – runs through each of these activities and realigned staff to reflect this common purpose. The board review and simulation courses continue to be successful, and a certification program for the ultrasound courses is under way.

PHOTOS COURTESY ACCP

FIRS meeting and launch of the Year of the Lung, Paris, January 2010.

At the Cutting Edge of Guidelines

We hosted (first time in North America) the Guidelines International Network (G-I-N) Conference in August 2010, an international effort to improve patient care through the development and implementation of clinical practice guidelines. The G-I-N Conference 2010 brought together professionals involved in evidence synthesis, guideline development, implementation, quality improvement, and health policy to integrate knowledge and improve patient outcomes. This highly successful conference is a testament to our leadership in the guidelines arena.

International Front

My theme for the year was "Care Locally, Reach Globally." In this context, Drs Gutterman, Raoof, and I, in the ACCP Presidential line, worked together to have a concerted effort for longevity, stability, and continuity. We are focusing our long-term international development on selected geographic regions – the Middle East, Latin America, India, and China – with significant potential. Different countries require different strategies, and we are planning our global initiatives accordingly. These have borne fruitful results that will have long-term implications. Keeping our prime directive mantra as "Budget-Neutral," the College partnered with international groups to bring our clinical education to those who cannot attend CHEST meetings. To that end, I had the privilege, along with other ACCP colleagues, to represent the College at several international meetings, including those in Abu Dhabi, Australia, Malaysia, Brazil, Argentina, Peru, France, Korea, Barcelona, Canada, Italy, China, Mexico, and Poland.

Forging New Partnerships

COPD Alliance: We agreed to be a founding member of the COPD Alliance, along with the American Academy of Nurse Practitioners, American Academy of Physician Assistants, American College of Osteopathic Family Physicians, American College of Osteopathic Internists, and American Osteopathic Association. One of the first action items for this multiyear, multimillion-dollar project is the development of COPD.org, a shared resource to house content on COPD awareness and management. With our core competency as education,

Continued on following page

Continued from previous page

we are exploring some exciting partnering opportunites in delivering today's education by tomorrow's methods!

The CHEST Foundation: "The Soul of the ACCP"

The CHEST Foundation undertook several key initiatives during the past year that will enable The Foundation to continue to impact more ACCP members and their patients.

Branding Campaign for The CHEST Foundation: After an initial strategic planning process, The Foundation developed a new brand and tag line, OneBreath: Make The Most Of It, designed to aggregate The Foundation's programs under three pillars: education, care, and community.

3rd Annual Case Competition: The CHEST Foundation, in collaboration with the Social Enterprise at Kellogg of the Kellogg School of Management, the Carol and Larry Levy Social Entrepreneurship Lab, and Medtronic Diabetes, sponsored the 3rd Annual Case Competition. The 2010 competition focused on development of a chronic care model for diabetes. Partners of this year's competition included the CDC Foundation and the American Diabetes Association.

Pro Bono Courses: The Pro Bono Committee of the Foundation (Paul Kvale, MD, FCCP, Chair) put together many pro bono courses in areas where there is a need for taking our education at minimal cost to the sponsoring country.

COURTESY ACCP

Meeting with ACCP Korean members at the Asian Pacific Society of Respirology (APSR) 2009 Congress, Seoul, Korea, November 2009.

The Ambassadors Group: This dedicated group continued to grow under the leadership of my husband, Jayarama Guntupalli, MD, as Chair. Key projects included a new partnership with the AMA Alliance focused on tobacco control and the dissemination of Ambassadors Group note cards. Several Ambassadors Group members presented tobacco prevention programs in their communities using The Foundation's Lung Lessons℠ program.

New Initiatives at CHEST 2010

More CME! In order to cater to the educational needs of our international attendees, for the first time, we are starting the CHEST 2010 conference a day earlier (on Sunday) with a full day of programming on "global health." International faculty will cover topics of global interest, including a session in Spanish. We hope to continue this in the coming years. We also have many more offerings in simulation.

In Conclusion

Our ACCP staff is an integral part of the success of the College. ACCP staff members work behind-the-scenes, making everything we do flow flawlessly. We unexpectedly lost one of those individuals, Mary Margaret Berg, Assistant Vice President of Medical Education and Accreditation, in March. Her passing is an enormous loss to her family and to her many ACCP friends and colleagues.

Throughout my presidency, I urged members and new Fellows to remain actively engaged in the ACCP. None of the above could have been accomplished without their countless hours of volunteer service. Thank you for your unwavering commitment to the College and for the opportunity to serve as your ACCP President. It has been my distinct honor and pleasure to pursue our new vision to be "the global leader in providing education in cardiopulmonary, critical care, and sleep medicine to optimize health and advance patient care." ■

November Lessons

▶ **Intraabdominal Hypertension and Abdominal Compartment Syndrome.** *By Dr James A. Barker, FCCP; and Dr Linda A. Perkins*

▶ **Irritant-Induced Asthma.** *By Dr Susan M. Tarlo, FCCP*

www.chestnet.org/accp/pccsu

PCCSU
PULMONARY, CRITICAL CARE, SLEEP UPDATE

Meet the New Ambassadors Group Chair: Kathleen Wilder

"Join for your interests and the camaraderie. Participate as you feel more comfortable, and carry the volunteer programs that energize you to your community."

So says the new Ambassadors Group Chair, Kathleen (Kathy) Wilder. Mirroring the goals of The CHEST Foundation, the ACCP Ambassadors Group reaches out to communities around the world to improve patient care and lung health. Newly appointed Ambassadors Group Chair, Kathy Wilder, exemplifies this work, having presented The CHEST Foundation's Lung Lessons℠ to over 7,000 4th, 5th, and 6th graders in her home state of Alaska. Kathy officially became the 2010-2011 Ambassadors Group Chair at CHEST 2010.

KATHLEEN WILDER, CHAIR

Kathy began her professional career as a math teacher and retired in 2000 from her position as Assistant Professor, University of Alaska, Anchorage, College of Business and Public Policy. Retirement gave Kathy time for family, volunteer work, and travel. She supports and shares the busy schedule of her husband, Norman Wilder, MD, FCCP, Chief Medical Officer at Alaska Regional Hospital. Kathy has two daughters, three granddaughters, and a fourth granddaughter due this month.

Prior to becoming Ambassadors Group Chair, Kathy implemented the "train the trainer" program to teach educators in Alaska how to present the Lung Lessons℠ program, enabling this important work to continue as she takes on the added responsibilities of Chair. Kathy enjoyed serving as Hospitality Committee Chair and Poster Contest Committee Chair, and she organized the first photo directories for the Ambassadors Group. She values the friendships that began and continue to grow through her participation in the Ambassadors Group events.

As Chair, Kathy aims to continue the established activities of The Ambassadors Group, such as the support of a humanitarian award and educational activities for young people about lung health. She would also like to see an emphasis on growing the membership.

Kathy welcomes all ACCP members and their families to join The Ambassadors Group. She urges those who may be a bit shy to observe for a time and gradually become more involved. ■

More information about The Ambassadors Group and Lung Lessons℠ is available at www.chestfoundation.org.

This Month in *CHEST*: Editor's Picks

BY DR RICHARD S. IRWIN, MASTER FCCP
Editor in Chief, CHEST

▶ **Patient-Controlled Sedation: A Novel Approach to Sedation Management for Mechanically Ventilated Patients.** *By Dr L. L. Chlan, et al.*

▶ **Survival in Sarcoidosis-Associated Pulmonary Hypertension: The Importance of Hemodynamic Evaluation.** *By Dr R. P. Baughman, et al.*

▶ **A Novel User-Friendly Score (HAS-BLED) To Assess 1-Year Risk of Major Bleeding in Patients With Atrial Fibrillation: The Euro Heart Survey.** *By Dr R. Pisters, et al.*

TRANSPARENCY IN HEALTH CARE

▶ **Reducing Iatrogenic Risks: ICU-Acquired Delirium and Weakness – Crossing the Quality Chasm.** *By Dr E. E. Vasilevskis, et al.*

POINT/COUNTERPOINT

▶ **Should We Abandon $FEV_1/FVC < 0.70$ To Detect Airway Obstruction?**
No. By Dr B. R. Celli and Dr R. J. Halbert
Yes. By Dr P. Enright and Dr V. Brusasco

SPECIAL FEATURE

▶ **Diagnostic Criteria for the Classification of Vocal Cord Dysfunction.** *By Dr M. J. Morris and Dr K. L. Christopher*

RECENT ADVANCES IN CHEST MEDICINE

▶ **Chronic Macrolide Therapy in Inflammatory Airways Diseases.** *By Dr A. L. Friedlander and Dr R. K. Albert*

www.chestpubs.org

SLEEP STRATEGIES

OSA in the Perioperative Setting

The prevalence of obstructive sleep apnea (OSA) in western countries is estimated at about 5%, though recent data suggest that 26% of the adult population may be at risk (Hiestand et al. *Chest.* 2006;130[3]:780). Despite increased recognition of this disorder and availability for testing, the overwhelming majority of cases (estimated at 80%) has not been diagnosed. OSA, characterized by the repetitive partial (hypopneas) or complete (apneas) collapse of the upper airway during sleep, has been associated with a variety of adverse health consequences. Aside from the chronic health effects, there is growing interest in the potential for acute worsening of OSA in the perioperative setting, resulting in poor patient outcomes. Case series from the 1990s suggested that patients with OSA undergoing general anesthesia could suffer serious adverse effects, including death, in the perioperative period. These reports were followed by well-controlled retrospective studies confirming that bad outcomes – including difficult mask ventilation, difficult or failed tracheal intubation, hypoxemia, postoperative airway obstruction, cardiac arrhythmias, and MI – were more likely in patients with OSA undergoing a variety of surgeries.

Individuals with OSA appear to be at increased risk for preoperative, intraoperative, and postoperative adverse events. Poor visualization of a crowded oropharynx may make airway control difficult, a problem further complicated by the effects of induction agents. The lingering effects of general anesthesia, neuromuscular relaxants, narcotics, and sedatives may all enhance pharyngeal muscle relaxation and depress the arousal response, resulting in more frequent and longer apneas postoperatively. Supine positioning, often required following surgery, and the potential for rapid eye movement (REM) rebound sleep after the first postoperative night can both lead to worsening of sleep apnea. Surgery and general anesthesia can unfavorably impact pulmonary function, impairing gas exchange and leading to hypoxemia that may be exacerbated during sleep.

Data suggest that the majority of postoperative complications occur in the first 72 h following surgery, mostly in the first 24 h (Gupta et al. *Mayo Clin Proc.* 2001;76[9]:897). The effects of anesthetics, narcotics, and surgery are likely responsible for the high complication rate seen early after surgery. Recent work suggests that the apnea-hypopnea index progressively increases over the 3 nights following surgery (Chung et al. *Sleep.* 2010;33:A126). This may help to explain late postoperative complications seen in patients with OSA. REM rebound sleep has also been suggested to play a role in OSA worsening later in the postoperative course. During REM rebound sleep, REM-associated hypoxemic episodes can increase threefold on the second and third nights compared with the night before surgery (Knill et al. *Anesthesiology.* 1990;73[1]:52).

Like the general population, most patients with OSA undergoing surgery have not been diagnosed prior to surgery. In a study of 2,877 elective surgery patients, 24% were found to be at risk for having OSA, and 81% of these had not been diagnosed (Finkel et al. *Sleep Med.* 2009;10[7]:753). This raises the question as to whether all patients undergoing elective surgery should be screened for OSA. A recent metaanalysis of clinical prediction tools for OSA found that, while the Berlin questionnaire and the Sleep Disorders Questionnaire were the most accurate questionnaires, and morphometry and combined clinical cephalometry were the most accurate clinical tools, all instruments showed poor reproducibility and significant false-negative rates, resulting in no single ideal screening test (Ramachandran and Josephs. *Anesthesiology.* 2009;110[4]:928). It can be argued that instead of identifying all patients with undiagnosed OSA preoperatively, identifying only those at risk for complications is more important. Two studies, one utilizing overnight oximetry preoperatively (Hwang et al. *Chest.* 2008; 133[5]:1128), and the other the sleep apnea clinical score coupled with witnessed respiratory events in recovery (Gali et al. *Anesthesiology.* 2009;110[4]: 869), suggest this may be the case.

The need for perioperative management guidelines for patients with OSA has been recognized by both the American Academy of Sleep Medicine and the American Society of Anesthesiology (ASA) in reviews on this topic. However, both acknowledge that there is currently little evidence to guide recommendations. With this in mind, the ASA has offered expert consensus guidelines for the perioperative care of patients with OSA, though these require validation (*Anesthesiology.* 2006;104[5]:1081). Interventions could be performed preoperatively, intraoperatively, or postoperatively.

In the preoperative setting, identifying known and suspected patients with OSA should help with planning airway management perioperatively. Some clinicians recommend awake intubation or use of fiberoptic intubation in patients with OSA due to the propensity for airway collapse with induction agents (Riley et al. *Otolaryngol Head Neck Surg.* 1997;117[6]:648). If induction prior to intubation is performed, reversal agents and fiberoptic equipment should be readily available.

Intraoperatively, potential advantages to the use of regional anesthesia in the patient with OSA include increased postoperative alertness, decreased requirement for opioids, and avoidance of tracheal intubation and airway instrumentation. However, general anesthesia is often required and, therefore, consideration should be given to using drugs that have minimal effect on respiration and/or are rapidly eliminated.

Most practitioners would agree that in patients with mild OSA undergoing minimally invasive procedures with little postoperative narcotic need, no specific additional monitoring is required postoperatively. Similarly, in patients with severe OSA undergoing major thoracic or abdominal surgical procedures with significant postoperative narcotic need, a higher level of monitoring is required. Unfortunately, the large gray zone between these extremes poses the greatest challenge with respect to postoperative decision-making in the vast majority of patients with OSA.

While not studied, some clinicians recommend extubation of patients with OSA only once fully awake. Complete recovery from neuromuscular blockade is required, and extubation should take place in the reverse Trendelenburg or semi-upright positions. Prolonged postanesthesia care unit (PACU) monitoring should be considered prior to discharge home or transfer to the inpatient unit. Patient-controlled analgesia with no basal rate and restricted dosing may limit narcotic dosing. Naloxone should be readily available in all cases. Sedatives should be avoided altogether in the postoperative setting if feasible. Positive pressure therapy (CPAP and bilevel pressure support) is the mainstay of treatment for OSA. However, there are no randomized controlled trials of the use of CPAP or bilevel pressure support in patients with OSA in the postoperative setting. Limited data suggest a possible benefit for those patients utilizing CPAP perioperatively (Gupta et al. *Mayo Clin Proc.* 2001;76[9]:897). Proper studies have yet to be performed to determine if self-adjusting CPAP devices would be beneficial for patients with OSA during the postoperative period. For some patients who adamantly refuse CPAP but are having difficulties, nasopharyngeal airways may offer some benefit.

The type and location of postoperative monitoring for patients with OSA is a difficult triage decision that will depend on a number of factors unique to each case. These factors generally include age, comorbidities, severity of the known sleep apnea, the nature of surgery, type of anesthesia, presence of PACU events, and need for postoperative narcotics. Unfortunately, there is little published data other than consensus guidelines available to help with this decision-making process. While many patients can be released after monitoring in the PACU, and some will clearly require ICU monitoring, how best to care for the remainder of the patients should be individualized, taking into account the factors mentioned.

In summary, patients with OSA subject to surgery appear to be at increased risk for perioperative complications. Perioperative caregivers need to be cognizant of this and the fact that most patients with OSA have not been diagnosed with the disorder. Preoperative screening for OSA requires further study to determine its impact on outcomes. Anesthesiologists need to be prepared for potential difficulty in managing the airway of these patients. Anesthetic, sedative, and analgesic drugs should be used with caution in patients with known or suspected OSA. Nasal CPAP before surgery and after extubation may improve outcomes in these patients, though further study is needed. Decisions regarding postoperative monitoring of patients with OSA should be tailored to the specifics of each case, though a conservative approach seems prudent for patient safety. ■

Dennis Auckley, MD, FCCP
Division of Pulmonary, Critical Care, and Sleep Medicine; and
Norman Bolden, MD,
Department of Anesthesiology
MetroHealth Medical Center
Case Western Reserve University
Cleveland, OH

Dr James Parish, FCCP
Section Editor,
Sleep Strategies

Product of the Month

ACCP-SEEK® Critical Care Medicine: Volume XX
ACCP-SEEK® Sleep Medicine: Second Edition

ACCP-SEEK products are designed to stimulate and challenge the learner's clinical thought processes regarding recall, interpretation, and problem-solving. The case-based questions contain histories, laboratory results, and images, and they provide education concerning current diagnostic and treatment strategies. Each volume contains questions, answers, and rationales. The rationales provide thorough explanations and reasoning for the correct and incorrect answers. The ACCP-SEEK series is an invaluable study tool for physicians interested in certifying and recertifying in sleep, pulmonary, and critical care subspecialties. Find ACCP-SEEK products in the ACCP Store at www.chestnet.org. ■

NSCLC Survival: Lymph Node Sampling vs. Dissection

BY MITCHEL L. ZOLER
Elsevier Global Medical News

TORONTO – Complete mediastinal lymph node dissection provided no more survival benefit than did aggressive lymph node sampling in patients with early-stage non–small cell lung cancer, according to results from a randomized, multicenter trial with more than 1,000 patients.

However, lymph node sampling missed N2 lymph node spread in 4% of the patients, and complete lymph node dissection allowed the diagnosis. Identifying such patients can improve their survival by triggering treatment with adjuvant chemotherapy. Thus, "we would still recommend lymph node dissection" for patients with resectable, non–small cell lung cancer (NSCLC) at stage T1 or T2, N0, or nonhilar N1, said Dr. Gail E. Darling at the annual meeting of the American Association for Thoracic Surgery. The findings do not apply to patients with higher-stage NSCLC or to those who did not undergo vigorous staging, she stressed.

Dr. Darling conceded that the extensive lymph node dissection routinely used in the current study "may not be applicable to the real world." Prior reports showed that less than half of patients who have surgery for NSCLC have mediastinoscopy/lymph node sampling before their cancer resection, and the new results cannot apply to patients who do not undergo systematic sampling, she said.

Median overall survival reached 8.1 years in the sampling-only group and 8.5 years in the dissection group.

DR. DARLING

"The studies that showed a survival benefit from lymph node dissection were in patients with no pre-resection lymph node sampling or staging," noted Dr. Darling, a general thoracic surgeon at the University of Toronto.

The study enrolled patients at 63 centers participating in the American College of Surgeons Oncology Group, and involved 102 general thoracic surgeons. The study included 1,023 patients eligible for analysis, with a median age of 68 years and an even gender split.

A total of three-quarters of the patients had surgical resection of their tumor by lobectomy. About 40% of the tumors in both the sampling and dissection subgroups were stage IA, 40% were stage IB, and the rest were stage IIA, IIB, IIIA, or IIIB. The most common form of NSCLC was adenocarcinoma.

All patients had extensive and systematic lymph node sampling. After sampling, 525 patients who were negative on sampling were randomized to additionally undergo lymph node dissections, and the other 498 patients who were negative on sampling had no further assessment.

At a median follow-up of 6.3 years, overall mortality was 42% in the patients who had node dissection and 44% in those with sampling only. Median overall survival was 8.1 years in the sampling-only group and 8.5 years in the dissection group. Neither difference was significant.

Dr. Darling said that she and her associates on the study had no disclosures. ■

Life Expectancy 1 Year Shorter

Lung Transplants • *from page 1*

giving the transplant recipients a net survival benefit of about 3 years.

Patients in the highest priority groups (LAS greater than 80) also experienced net survival benefits, although not as great as those in the moderate priority group. Without a transplant, median survival for these patients on the waiting list was just 7-14 days. With the transplant, they live a median of about 2 years.

Patients whose LAS was less than 50 accounted for 88.2% of the candidates and 89.4% of the recipients. "There are probably about 350 patients in the higher priority groups who died on the waiting list," Dr. Russo said. "So you have to wonder why we're transplanting patients in the lowest priority group when there are patients in the higher priority group who die on the waiting list."

Dr. Russo continued, "This is not meant to represent a criticism of the LAS. I think it's a great step forward. [But] the current LAS system is largely based on the idea that medical urgency is weighted more heavily than posttransplant survival. If patients in the highest priority groups are expected to have the worst outcomes … that may prevent our maximizing the benefits of the organs that are available. And I think that's a question that potentially needs to be readdressed."

In an interview, Dr. Russo suggested that broadening the geographic area within which organs are shared may improve matters. At present, if there is no high-priority patient on the waiting list who is a match for an available lung, that lung will go to another nearby patient with a lower priority rather than to a higher priority patient farther away.

In discussing the lack of net survival benefit for lung recipients in the low-priority group, Dr. Russo acknowledged that the investigators were unable to include quality of life measures along with quantity of life measures in their analysis.

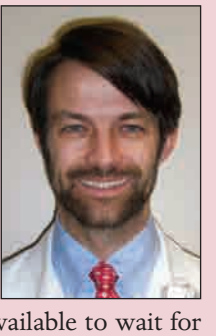
Although a low-priority patient who receives a lung may, on average, have a somewhat shorter life span than would a similarly low-priority patient who remains on the waiting list, the transplant recipient may enjoy a significantly better quality of life, he said.

"Dr. Russo's work addresses an important question, given the ongoing difficulties with scarcity of resources in transplantation, particularly in lung transplantation," said Dr. Michael A. Smith, a thoracic surgeon at St. Joseph's Hospital and Medical Center, Phoenix.

"Two recent studies have shown that although lung transplantation substantially improves quality of life, it has limited cost-effectiveness. In reaction to the difficult economic environment that we face today, some payers – including the Medicaid system of my home state of Arizona – have determined that because of limited survival advantages and poor cost-effectiveness, they will no longer cover lung transplantation for most patients," he said in an interview. ■

COMMENTARY

Dr. Joseph Barney, FCCP, comments: I think this article reflects the impact of LAS scoring on patients receiving organs, and is probably a reflection of the fact that we also need not lose sight of improving medical care of patients with illness such as advanced COPD and cystic fibrosis to the point that they survive longer without transplantation in general, and more specifically, have more time available to wait for organ availability.



Snoring in Pregnancy Linked to Gestational Diabetes

BY BRUCE JANCIN
Elsevier Global Medical News

SAN ANTONIO – Women who snore frequently during pregnancy are at elevated risk for gestational diabetes mellitus, according to a case-control study.

Although the risk is particularly high in obese snorers, snoring remained an independent risk factor for developing gestational diabetes even after controlling for body mass index, Louise M. O'Brien, Ph.D., said at the annual meeting of the Associated Professional Sleep Societies.

"These findings have important implications for the prevention of an event – gestational diabetes mellitus – and all its associated morbidities. I have to believe there is a role for patient education and screening: asking pregnant women about their sleep and especially about their snoring in order to improve pregnancy outcomes," said Dr. O'Brien of the department of neurology at the University of Michigan, Ann Arbor.

She reported on 1,221 women in their third trimester who completed questionnaires about habitual snoring, which was defined as snoring 3 or more nights per week. Nearly 31% of the women were habitual snorers in their last trimester. Their mean response to a screening 1-hour oral glucose tolerance test (OGTT) was a blood glucose level of 124 mg/dL, significantly higher than the 117 mg/dL in nonsnorers. Of the frequent snorers, 37% had a response of 130 mg/dL or more, compared with 30% of nonsnorers.

A formal diagnosis of gestational diabetes mellitus was made in 24% of the habitual snorers and 17% of nonsnorers, a significant difference.

Altogether, 37% of study participants were obese in their third trimester. Habitual snorers were more likely to be obese. Gestational diabetes was diagnosed in 34.5% of obese habitual snorers and 13% of nonobese nonsnorers.

In a multivariate regression analysis adjusted for age, race, gestational age, and parity, obese snorers were at 3.6-fold increased risk of developing gestational diabetes, compared with nonobese nonsnorers. Upon controlling further for body mass index, habitual snoring in pregnancy remained independently associated with a significant 1.5-fold increased rate of gestational diabetes.

Dr. O'Brien noted that this finding of an increased risk of gestational diabetes associated with snoring was independently confirmed in two other recent studies.

Physicians at Northwestern University in Chicago reported in a prospective sleep survey study of 189 healthy nulliparas that 18.5% of them snored at least 3 nights per week. Their mean 1-hour OGTT values were significantly higher than nonsnorers' (118 vs. 108 mg/dL). Their 14.3% incidence of gestational diabetes was significantly higher than the 3.3% rate in nonsnorers, as well. The 48% of women who averaged less than 7 hours of sleep per night had a 10.2% incidence of gestational diabetes, compared with 1.1% in those who slept at least 7 hours (Am. J. Obstet. Gynecol. 2010;203:142.e1-5).

In the other study, investigators at Seattle's Swedish Medical Center interviewed 1,290 women early in pregnancy regarding sleep duration and snoring. Their incidence of gestational diabetes was 5.3%.

Women who reported sleeping an average of 4 hours or less per night had a 5.6-fold greater rate of gestational diabetes than those who slept 9 hours. Overweight short sleepers had a 9.8-fold increased risk. Overweight women who snored at least 3 nights per week had a 6.9-fold increased gestational diabetes incidence, compared with normal-weight nonsnorers (BMC Womens Health 2010;10:17).

Dr. O'Brien reported having no financial conflicts. ■

COMMENTARY

Dr. Paul Selecky, FCCP, comments: Fascinating findings. We also know that snoring during pregnancy is associated with a higher incidence of low-birth-weight infants and preeclampsia. Presumably, the snoring was a sign of undiagnosed obstructive sleep apnea.

TYGACIL is in the 2009 IDSA/SIS guidelines for cIAI and the 2009 SIS guidelines for cSSSI.[1,2]

Expanded broad-spectrum coverage[3]* is on your side

***TYGACIL does not cover *Pseudomonas aeruginosa*.**

TYGACIL is indicated for the treatment of adults with:

- **Complicated skin and skin structure infections** caused by *Escherichia coli, Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus agalactiae*, *Streptococcus anginosus* grp. (includes *S. anginosus, S. intermedius*, and *S. constellatus*), *Streptococcus pyogenes*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Bacteroides fragilis*
- **Complicated intra-abdominal infections** caused by *Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Clostridium perfringens*, and *Peptostreptococcus micros*
- **Community-acquired bacterial pneumonia** caused by *Streptococcus pneumoniae* (penicillin-susceptible isolates), including cases with concurrent bacteremia, *Haemophilus influenzae* (beta-lactamase negative isolates), and *Legionella pneumophila*

Important Safety Information

- TYGACIL is contraindicated in patients with known hypersensitivity to tigecycline
- Anaphylaxis/anaphylactoid reactions have been reported with nearly all antibacterial agents, including tigecycline, and may be life-threatening. TYGACIL should be administered with caution in patients with known hypersensitivity to tetracycline-class antibiotics
- Isolated cases of significant hepatic dysfunction and hepatic failure have been reported in patients being treated with tigecycline. Some of these patients were receiving multiple concomitant medications. Patients who develop abnormal liver function tests during tigecycline therapy should be monitored for evidence of worsening hepatic function. Adverse events may occur after the drug has been discontinued
- The safety and efficacy of TYGACIL in patients with hospital-acquired pneumonia have not been established
- **An increase in all-cause mortality has been observed across phase 3 and 4 clinical studies in TYGACIL-treated patients versus comparator-treated patients. The cause of this increase has not been established. This increase in all-cause mortality should be considered when selecting among treatment options**
- **TYGACIL may cause fetal harm when administered to a pregnant woman**
- **The use of TYGACIL during tooth development may cause permanent discoloration of the teeth.** TYGACIL should not be used during tooth development unless other drugs are not likely to be effective or are contraindicated
- Acute pancreatitis, including fatal cases, has occurred in association with tigecycline treatment. Consideration should be given to the cessation of the treatment with tigecycline in cases suspected of having developed pancreatitis
- *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including TYGACIL, and may range in severity from mild diarrhea to fatal colitis
- Monotherapy should be used with caution in patients with clinically apparent intestinal perforation
- TYGACIL is structurally similar to tetracycline-class antibiotics and may have similar adverse effects. Such effects may include: photosensitivity, pseudotumor cerebri, and anti-anabolic action (which has led to increased BUN, azotemia, acidosis, and hyperphosphatemia). As with tetracyclines, pancreatitis has been reported with the use of TYGACIL
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of TYGACIL and other antibacterial drugs, TYGACIL should be used only to treat infections proven or strongly suspected to be caused by susceptible bacteria. As with other antibacterial drugs, use of TYGACIL may result in overgrowth of non-susceptible organisms, including fungi
- The most common adverse reactions (incidence >5%) are nausea, vomiting, diarrhea, abdominal pain, headache, and increased SGPT
- Prothrombin time or other suitable anticoagulant test should be monitored if TYGACIL is administered with warfarin
- Concurrent use of antibacterial drugs with oral contraceptives may render oral contraceptives less effective
- The safety and effectiveness of TYGACIL in patients below age 18 and lactating women have not been established

Please see brief summary of Prescribing Information on adjacent page.

References: 1. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50:133-164. **2.** May AK, Stafford RE, Bulger EM, et al. Treatment of complicated skin and soft tissue infections. *Surg Infect*. 2009;10:467-499. **3.** TYGACIL® (tigecycline) Prescribing Information, Wyeth Pharmaceuticals Inc.

Pfizer

Tygacil® tigecycline IV

Expanded broad-spectrum coverage