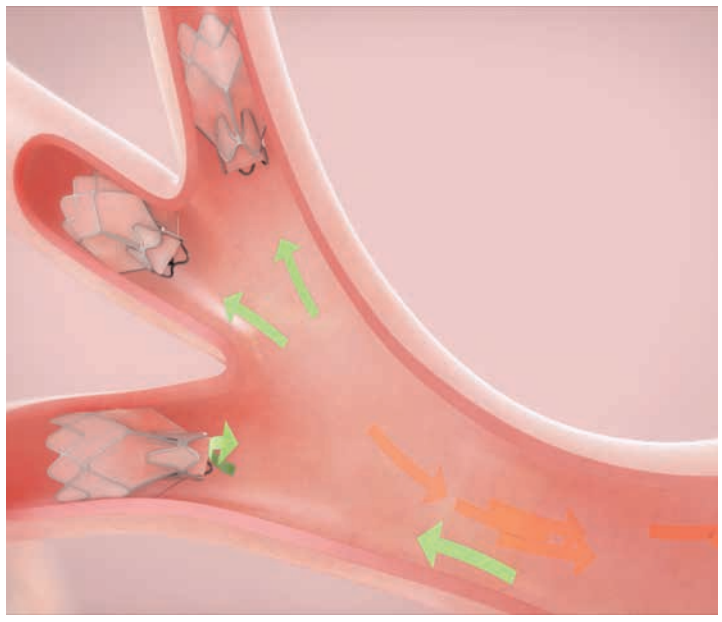
Celebrating 10 Years
VOL. 11 • NO. 1 • JANUARY 2016

CHEST® Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS



COURTESY PULMONX, INC.

Endobronchial valves boost lung function

BY MARY ANN MOON
Frontline Medical News

Endobronchial valves improved pulmonary function, exercise capacity, and quality of life in a prospective randomized controlled trial involving 68 adults with severe emphysema, according to a report published in the New England Journal of Medicine.

"The improvements we found were of greater magnitude than those noted with pharmacologic treatment in comparable patients and were similar to improvements with surgical lung-volume reduction, but with significantly less morbidity," said Karin Klooster of the department of pulmonary diseases, University Medical Center Groningen (the Netherlands) and her associates.

Previous research suggested that bronchoscopic lung-volume reduction using one-way endobronchial valves to block inspiratory but not expiratory air flow would be most effective in patients who had a complete rather than an incomplete fissure between the targeted lobe and the adjacent lobe on high-resolution CT.

"A complete fissure on HRCT [high-resolution computed tomography] is a surrogate finding for the absence of interlobar collat-

See **Valves** • *page 7*

COPD doubled risk of sudden cardiac death in LIFE trial

Lowering BP did not negate risk.

BY BRUCE JANCIN
Frontline Medical News

ORLANDO – A second, confirmatory major study has shown that chronic obstructive pulmonary disease independently increases the risk of sudden cardiac death severalfold.

COPD was associated with a roughly twofold increased risk of sudden cardiac death (SCD) in hypertensive patients with COPD, compared with those without the pulmonary disease, in the Scandinavian Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) trial, Dr. Peter M. Okin reported at the American Heart Association scientific sessions.

Moreover, aggressive blood pressure lowering in the hypertensive COPD patients didn't negate this risk, added Dr. Okin of Cornell University in New York.

The impetus for his secondary analysis of LIFE data was an earlier report from the landmark, population-based Rotterdam Heart Study.

Among 1,615 participants with COPD, the age- and sex-adjusted risk of SCD was

See **LIFE** • *page 5*

INSIDE

Guidelines recommend NOACs over warfarin for initial VTE treatment

In this latest evidence-based guideline chapter, called *Antithrombotic Therapy for VTE Disease: CHEST Guideline, from the American College of Chest Physicians*, experts provide 53 updated recommendations for the appropriate treatment of patients who have venous thromboembolism.

Key changes from the 9th edition to the 10th edition include the following recommendations:

• Non-vitamin K antagonist oral anticoagulants (NOACs) are recommended over warfarin for initial and long-term treatment of VTE in patients without cancer.

• Compression stockings are out in acute DVT

• New subsegmental pulmonary embolism treatment recommendations.

The complete guideline chapter is free to view in the January 2016 "Online First" section of the journal *CHEST* at http://journal.publications.chestnet.org.

CHEST Physician
151 Fairchild Ave.,
Suite 2,
Plainview, NY 11803-1709

CHANGE SERVICE REQUESTED

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

Indication

Esbriet® (pirfenidone) is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

Select Important Safety Information

Elevated liver enzymes: Increases in ALT and AST >3× ULN have been reported in patients treated with Esbriet. Rarely these have been associated with concomitant elevations in bilirubin. Patients treated with Esbriet had a higher incidence of elevations in ALT or AST than placebo patients (3.7% vs 0.8%, respectively). No cases of liver transplant or death due to liver failure that were related to Esbriet have been reported. However, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that could lead to death or the need for liver transplants in some patients. Conduct liver function tests (ALT, AST, and bilirubin) prior to initiating Esbriet, then monthly for the first 6 months and every 3 months thereafter. Dosage modifications or interruption may be necessary.

Photosensitivity reaction or rash: Patients treated with Esbriet had a higher incidence of photosensitivity reactions (9%) compared with patients treated with placebo (1%). Patients should avoid or minimize exposure to sunlight (including sunlamps), use a sunblock (SPF 50 or higher), and wear clothing that protects against sun exposure. Patients should avoid concomitant medications that cause photosensitivity. Dosage reduction or discontinuation may be necessary.

Gastrointestinal disorders: Gastrointestinal events of nausea, diarrhea, dyspepsia, vomiting, gastroesophageal reflux disease, and abdominal pain were more frequently reported in patients treated with Esbriet. Dosage reduction or interruption for gastrointestinal events was required in 18.5% of patients in the Esbriet 2403 mg/day group, as compared to 5.8% of patients in the placebo group; 2.2% of patients in the Esbriet 2403 mg/day group discontinued treatment due to a gastrointestinal event, as compared to 1.0% in the placebo group. The most common (>2%) gastrointestinal events that led to dosage reduction or interruption were nausea, diarrhea, vomiting, and dyspepsia. Dosage modifications may be necessary in some cases.

Adverse reactions: The most common adverse reactions (≥10%) were nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastroesophageal reflux disease, sinusitis, insomnia, weight decreased, and arthralgia.

Drug interactions: Concomitant administration with strong inhibitors of CYP1A2 (eg, fluvoxamine) significantly increases systemic exposure of Esbriet and is not recommended. Discontinue prior to administration of Esbriet. If strong CYP1A2 inhibitors cannot be avoided, dosage reductions of Esbriet are recommended. Monitor for adverse reactions and consider discontinuation of Esbriet as needed.

Start preserving more lung function for patients with IPF[4]

- Esbriet had a significant impact on lung function vs placebo in ASCEND[3,4†]
  - —**48% relative reduction in risk of a meaningful decline in lung function at 52 weeks for patients on Esbriet** vs placebo (17% vs 32%; 15% absolute difference; *P*<0.001)
  - —**2.3× as many patients on Esbriet maintained their baseline function at 52 weeks** vs placebo (23% vs 10% of patients; 13% absolute difference; *P*<0.001)
- Esbriet delayed progression of IPF vs placebo through a sustained impact on lung function decline in ASCEND[3,4†]
  - —**Patients on Esbriet maintained an average of 193 mL more lung function at 52 weeks** vs placebo (–235 mL vs –428 mL; *P*<0.001)
- **No statistically significant difference vs placebo in change in %FVC or decline in FVC volume from baseline to 72 weeks was observed in CAPACITY 006**[3,5]
- Esbriet has been approved outside the US since 2011, with approximately 15,000 patients treated with pirfenidone worldwide[2]

Learn more about Esbriet and how to access medication at EsbrietHCP.com.

ATS=American Thoracic Society; ERS=European Respiratory Society; JRS=Japanese Respiratory Society; ALAT=Latin American Thoracic Association; %FVC=percent predicted forced vital capacity.

*Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences.

†The efficacy of Esbriet was evaluated in three phase 3, randomized, double-blind, placebo-controlled trials. In ASCEND, 555 patients with IPF were randomized to receive Esbriet 2403 mg/day or placebo for 52 weeks. Eligible patients had %FVC between 50%-90% and $\%DL_{CO}$ between 30%-90%. The primary endpoint was change in %FVC from baseline to week 52.

Concomitant administration of Esbriet and ciprofloxacin (a moderate inhibitor of CYP1A2) moderately increases exposure to Esbriet. If ciprofloxacin at the dosage of 750 mg twice daily cannot be avoided, dosage reductions are recommended. Monitor patients closely when ciprofloxacin is used.

Agents that are moderate or strong inhibitors of both CYP1A2 and CYP isoenzymes involved in the metabolism of Esbriet should be avoided during treatment.

The concomitant use of a CYP1A2 inducer may decrease the exposure of Esbriet, and may lead to loss of efficacy. Concomitant use of strong CYP1A2 inducers should be avoided.

Specific populations: Esbriet should be used with caution in patients with mild to moderate (Child-Pugh Class A and B) hepatic impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Esbriet as needed. The safety, efficacy, and pharmacokinetics of Esbriet have not been studied in patients with severe hepatic impairment. Esbriet is not recommended for use in patients with severe (Child-Pugh Class C) hepatic impairment.

Esbriet should be used with caution in patients with mild (CL_{cr} 50-80 mL/min), moderate (CL_{cr} 30-50 mL/min), or severe (CL_{cr} less than 30 mL/min) renal impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Esbriet as needed. The safety, efficacy, and pharmacokinetics of Esbriet have not been studied in patients with end-stage renal disease requiring dialysis. Use of Esbriet in patients with end-stage renal disease requiring dialysis is not recommended.

Smoking causes decreased exposure to Esbriet, which may alter the efficacy profile of Esbriet. Instruct patients to stop smoking prior to treatment with Esbriet and to avoid smoking when using Esbriet.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

Please see Brief Summary of Prescribing Information on adjacent pages for additional Important Safety Information.

References: 1. Raghu G, Rochwerg B, Zhang Y, et al; ATS, ERS, JRS, and ALAT. An official ATS/ERS/JRS/ALAT clinical practice guideline: treatment of idiopathic pulmonary fibrosis. An update of the 2011 clinical practice guideline. *Am J Respir Crit Care Med.* 2015;192(2):e3-e19. **2.** Data on file. Genentech, Inc. **3.** Esbriet Prescribing Information. InterMune, Inc. October 2014. **4.** King TE Jr, Bradford WZ, Castro-Bernardini S, et al; for the ASCEND Study Group. A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis [published correction appears in *N Engl J Med.* 2014;371(12):1172]. *N Engl J Med.* 2014;370(22):2083-2092. **5.** Noble PW, Albera C, Bradford WZ, et al; for the CAPACITY Study Group. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. *Lancet.* 2011;377(9779):1760-1769.

Genentech
A Member of the Roche Group

Esbriet® (pirfenidone) capsules 267 mg | START HERE

Sugammadex OK'd to reverse neuromuscular block

BY M. ALEXANDER OTTO

The Food and Drug Administration has approved sugammadex (Bridion, Merck) injection to reverse the effects of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide.

The safety and efficacy of sugammadex were evaluated in three phase III trials involving 456 participants; most recovered within 5 minutes. An FDA review of the drug found that there was less residual neuromuscular blockade with sugammadex compared to neostigmine, and a 4-minute time savings to extubation and operating room discharge.

Sugammadex is a new molecular entity of the gamma-cyclodextrin class, designed to bind rocuronium and vecuronium.

aotto@frontlinemedcom.com

COPD boosts risk of sudden death

LIFE *from page 1*

1.34-fold greater than in nearly 12,000 controls.

This increased SCD risk climbed to 2.12-fold during the first 2,000 days following diagnosis of COPD and reached 3.58-fold among those with frequent COPD exacerbations during this period (Eur Heart J. 2015 Jul 14;36[27]:1754-61).

Dr. Okin's secondary analysis of the LIFE data included 9,193 hypertensive subjects with ECG evidence of left ventricular hypertrophy who were randomized to lisinopril- or atenolol-based blood pressure lowering to a target of 140/90 mm Hg or less.

A history of COPD was present in 385 patients (4.2%) at enrollment.

During a mean 4.8 years of prospective follow-up, 178 patients experienced SCD, a prespecified secondary endpoint in the LIFE trial.

The incidence rate was 9 cases per 1,000 patient-years in those with COPD and 3.8 per 1,000 person-years in those without the pulmonary disease.

In a univariate analysis, a history of COPD was associated with a 2.36-fold increased risk of SCD during follow-up.

In a multivariate analysis extensively adjusted for potential confounders – treatment arm, age, race, gender, history of atrial fibrillation, baseline serum creatinine and serum glucose, stroke or TIA, as well as on-treatment blood pressure, heart rate, QRS duration, HDL cholesterol level, use of a statin or hydrochlorothiazide, and incident MI or heart failure – COPD remained associated with a 1.82-fold increased risk of SCD, the cardiologist reported.

These results suggest the need for studies to assess if targeted therapies can reduce the SCD risk.

DR. OKIN

"These results suggest the need for additional studies to assess whether there are targeted therapies that can reduce the risk of SCD in patients with COPD," Dr. Okin concluded.

As previously reported, the main finding in LIFE was that losartan conferred benefits beyond blood pressure control (Lancet. 2002 Mar 23;359[9311]:995-1003).

bjancin@frontlinemedcom.com

VIEW ON THE NEWS

Dr. Vera A. De Palo, MBA, FCCP, comments: It has long been understood that nocturnal hypoxemia carries greater risk for cardiac events in patients. The findings from the Rotterdam Heart Study of a higher-than-control group risk for sudden cardiac death in COPD patients, with a higher risk within about 5 years of diagnosis of COPD and an even higher risk in COPD patients with frequent exacerbations, served as the impetus for the secondary analysis of data from the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) trial. This analysis of the more than 9000 hypertensive subjects demonstrated that there was a higher incidence of sudden cardiac death in patients with a history of COPD.

Panel advises reslizumab be approved for adults

BY DEEPAK CHITNIS
Frontline Medical News

SILVER SPRING, MD. – Reslizumab, a humanized monoclonal antibody, has been recommended for approval for the treatment of asthma and elevated blood eosinophils in patients aged 18 years and older by an advisory committee to the Food and Drug Administration.

Members of the FDA Pulmonary-Allergy Drugs Advisory Committee voted 11-3 to recommend the approval for adults, but unanimously voted "no" on the recommendation for approval for patients aged 12-17 years.

The advisers were tasked to consider a dosage of 3 mg/kg of reslizumab, administered intravenously once every 4 weeks for the management of severe asthma.

The panel members considered data culled from a sample population of 19 patients and other results to be insufficient evidence of significant benefit to adolescents.

"All of the evidence was going in the wrong direction" for the approval in patients 12-17 years old, according to panel member Erica H. Brittain, Ph.D., of the National Institute of Allergy and Infectious Diseases, Bethesda, Md.

FDA NEWS

A larger study, and one that includes patients young than age 12, is needed, said panelist Dr. Thomas A.E. Platts-Mills, professor of medicine at the University of Virginia, Charlottesville.

The advisory panel members considered data from five trials evaluating the safety and efficacy of reslizumab, which if approved would be marketed as Cinqair by Teva Pharmaceuticals.

Those trials included two 16-week lung-function studies examining forced expiratory volume in 1 second (FEV_1), two year-long asthma exacerbation studies, and an open-label safety extension study.

Advisers generally agreed that reslizumab demonstrated substantial improvement in FEV_1 and asthma exacerbation in the adult population. Specifically, in the two exacerbation studies, clinical asthma exacerbations did not occur over the 12-month study in 61% and 73% of subjects on reslizumab, vs. 44% and 52% of subjects in the control cohort, respectively.

However, panelists voiced concerns about the risks of muscle toxicity and, especially, anaphylaxis.

In a presentation regarding the treatment's immunogenicity issues, João A. Pedras-Vasconcelos, Ph.D., of the FDA Office of Pharmaceutical Quality, cautioned that not enough work was done by the sponsors to "thoroughly investigate [the] root causes of anaphylaxis."

Ultimately, the advisory committee largely agreed that the unmet need for reslizumab outweighed the potential risks.

In casting his "yes" vote regarding the adequacy of reslizumab's safety profile, panel chair Dr. Dennis R. Ownby, professor of pediatrics at Georgia Regents University in Augusta, said that he was "reluctant" to endorse reslizumab, but that he believes "this is a drug that clinicians will use very cautiously, [so] I'm placing faith on our practicing physicians" to prescribe the drug in a responsible manner.

Clinical asthma exacerbations did not occur over the 12-month study in 61% and 73% of subjects on reslizumab, vs. 44% and 52% of subjects in the control cohort, respectively.

Advisers voted 11-3 to recommend approval of reslizumab as a safe and effective treatment of severe asthma and elevated blood eosinophils. If approved by the FDA, reslizumab would be the third monoclonal antibody approved to treat asthma.

The FDA is not required to follow the advice of its advisory panels, but often does. No members of the panel reported any relevant financial conflicts of interest.

dchitnis@frontlinemedcom.com

IN THIS ISSUE

CHEST Physician Is Online
CHEST Physician is available on the Web at chestphysician.org

Dr. Vera A. De Palo, MBA, FCCP, is Medical Editor in Chief of *CHEST* Physician.

CHEST™ Physician
THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

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 CHEST members. Content for **CHEST Physician** is provided by Frontline Medical Communications Inc. Content for News From Chest is provided by the American College of Chest Physicians.

POSTMASTER: Send change of address (with old mailing label) to CHEST Physician, Subscription Service, 151 Fairchild Ave., Suite 2, Plainview, NY 11803-1709.

CHEST Physician (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609. Subscription price is $230.00 per year. Phone 973-206-3434, fax 973-206-9378.

Editorial Offices 5635 Fishers Lane, Suite 6100, Rockville, MD 20852, 240-221-2400, fax 240-221-2548
Advertising Offices 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609 973-206-3434, fax 973-206-9378

Scan this QR Code to visit chestnet.org/chestphysician

Frontline Medical Communications Society Partners
VP/Group Publisher; Director, FMC Society Partners Mark Branca
Editor in Chief Mary Jo M. Dales
Executive Editors Denise Fulton, Kathy Scarbeck
Creative Director Louise A. Koenig
Print Production Manager Rebecca Slebodnik
Senior Director of Classified Sales Tim LaPella, 484-921-5001, tlapella@frontlinemedcom.com
Display Advertising Managers Lauren Provenzano, 609-306-5776, lprovenzano@americanmedicalcomm.com, Michael O'Brien, 978-578-4514, mobrien@americanmedicalcomm.com
Classified Sales Representative Lauren Morgan 267-980-6087, lmorgan@americanmedicalcomm.com

Asthma history boosts heart risks after menopause

BY BRUCE JANCIN
Frontline Medical News

ORLANDO – A history of asthma was independently associated with a 24% increase in the risk of new-onset coronary heart disease among postmenopausal women in an analysis from the Women's Health Initiative.

The study cohort included 90,168 women aged 50-79 years who were free of cardiovascular disease at enrollment in the Women's Health Initiative (WHI), of whom 6,921 reported a history of physician-diagnosed asthma at baseline.

During follow-up in the prospective study, the incidence of a coronary heart disease event was 8.6% in subjects with a history of asthma and 6.97% in the subjects without a history of asthma, Dr. Fady Y. Marmoush reported at the American Heart Association scientific sessions.

Moreover, the incidence of a first cardiovascular event was 11.6% in the asthma group, compared with 9.7% in the controls without asthma, added Dr. Marmoush of Memorial Hospital of Rhode Island, Pawtucket.

Additionally, the asthma group had an absolute 1%-2% greater baseline prevalence of hypertension, diabetes, and a family history of coronary heart disease.

Those with asthma also were more likely to be obese. On the other hand, they were less likely to have ever smoked.

In a multivariate analysis adjusted for these and other potential confounders, including age, dyslipidemia, and waist-hip ratio, the women with a history of asthma had a 24% greater risk of coronary heart disease during prospective follow-up in the WHI, as well as a 21% increased rate of cardiovascular events, including stroke, compared with the no-asthma group.

Thus, a history of asthma could be a useful consideration – a tie breaker of sorts – in older women whose calculated 10-year atherosclerotic cardiovascular disease risk based on the standard risk factors places them on the borderline as candidates for statin therapy.

The most likely mechanism that accounts for the observed association between asthma history and increased risk of cardiovascular disease is the chronic inflammatory state that is a hallmark of asthma.

The condition likely accelerates the atherosclerotic process, which also is inflammatory, she said.

bjancin@frontlinemedcom.com

VIEW ON THE NEWS

Dr. Vera A. De Palo, MBA, FCCP, comments: Data from the Women's Health Initiative's prospective cohort study continues to place into perspective the importance of cardiovascular disease in women. This study advances the understanding of the importance of an underlying chronic asthma condition as an additional risk, as high as 25%, for cardiovascular disease. This knowledge can be useful in deciding treatment considerations.

Bruce Jancin/Frontline Medical News

Results rival those of surgery

Valves *from page 1*

eral ventilation; if there is collateral ventilation, an occluded lobe can be reinflated through its collaterals," defeating the purpose of the procedure, the researchers wrote.

During a 3-year period, Ms. Klooster and her associates studied emphysema patients who were older than 35 years (mean age, 58-59 years).

All had a postbronchodilator forced expiratory volume in 1 second (FEV_1) that was less than 60% of predicted volume, a total lung capacity that was more than 100% of the predicted value, and a residual volume that was more than 150% of predicted volume.

On HRCT, all the study participants had a complete or nearly complete fissure between the targeted lobe and the adjacent lobe.

The study subjects were randomly assigned to receive endobronchial valves (34 patients) or to usual care (34 control subjects) and their outcomes were followed for 6 months.

At the 6 month mark, control subjects were allowed to crossover and to receive endobronchial valves as well.

The median procedure time was 18 minutes (range, 6-51 minutes), and the median number of valves placed in each patient was 4 (range, 2-7 valves). The median hospital stay was 1 day (range, 1-13 days).

Compared with control subjects, patients who received endobronchial valves showed a reduction in target lobar volume of 1,366 mL.

This reduction was accompanied by improvements in FEV_1 by 191 mL, in forced vital capacity by 442 mL, in residual lung volume, in longer 6-minute walk distance by 106 meters, in scores on the Clinical COPD Questionnaire measuring daily functioning, and in scores on the St. George's Respiratory Questionnaire, which is a measure of quality of life.

The results for the control subjects who crossed over to the active-treatment group were similar (N Engl J Med. 2015 Dec 10;373:2325-35. doi:10.1056/NEJMoa1507807).

However, several adverse effects occurred, and close monitoring of this patient population is crucial, the researchers said. The most common complication was pneumothorax, which developed in 6 of the 34 patients (18%), usually within 1 day of undergoing the procedure.

Pneumothorax resolved spontaneously in one patient but required chest-tube drainage in the other five; it resolved in one patient after temporary removal of the valves to promote healing, and in another after permanent removal of all valves. Other adverse effects, some of which required repeat bronchoscopy, included torsion of the lower-lobe bronchus after upper-lobe treatment (two patients), pneumonia distal to the valves (one patient), increased dyspnea and sputum production (two patients), valve migration (two patients), valve dislocation because of granulation-tissue formation (one patient), and persistent cough (one patient). Despite these adverse events, "the overall outcome of treatment was positive," Ms. Klooster and her associates wrote.

All patients who underwent valve removal recovered without any further adverse effects, indicating that this treatment "is fully reversible and doesn't preclude further therapeutic options," they added.

VIEW ON THE NEWS

Dr. Vera A. De Palo, MBA, FCCP, comments: This study suggests that endobronchial valves hold promise for improved lung function and quality of life in COPD patients with air trapping and hyperinflation. Approximately 20% of patients had complications of the procedure ranging from cough and increased sputum production, to tortion of the lower-lobe bronchus in patients whose procedure was located at an upper lobe, to pnemonthorax, the most common of the complications. As with all procedures, the benefits of the procedure are to be weighed against the risks.

Three measures risk stratify acute heart failure

BY MITCHEL L. ZOLER
Frontline Medical News

ORLANDO – Three simple, routinely collected measurements together provide a lot of insight into the risk faced by community-dwelling patients hospitalized for acute decompensated heart failure, according to data collected from 3,628 patients at one U.S. center.

The three measures are blood urea nitrogen (BUN), systolic blood pressure, and serum creatinine. Using dichotomous cutoffs first calculated a decade ago, these three parameters distinguish up to an eightfold range of postdischarge mortality during the 30 or 90 days following an index hospitalization, and up to a fourfold range of risk for rehospitalization for heart failure during the ensuing 30 or 90 days, Dr. Sithu Win said at the American Heart Association scientific sessions.

Applying this three-measure assessment to patients hospitalized with acute decompensated heart failure "may guide care-transition planning and promote efficient allocation of limited resources," said Dr. Win, a cardiologist at the Mayo Clinic in Rochester, Minn. The next step is to try to figure out the best way to use this risk prognostication in routine practice, he added.

Researchers published the original analysis that identified BUN, systolic BP, and serum creatinine as key prognostic measures in 2005 using data taken from more than 65,000 U.S. heart failure patients enrolled in ADHERE (Acute Decompensated Heart Failure National Registry) (JAMA. 2005 Feb 2;293[5]:572-80). Using a classification and regression tree analysis, the 2005 study verified dichotomous cutoffs for these three parameters that identified patients at highest risk for in-hospital mortality.

The 2005 study prioritized the application of these cutoffs to define in-hospital mortality risk: first BUN, then the systolic BP criterion, and lastly the serum creatinine criterion. This resulted in five risk levels: Highest-risk patients had a BUN of at least 43 mg/dL, a systolic BP of less than 115 mm Hg, and a serum creatinine of at least 2.75 mg/dL. Lowest-risk patients had a BUN of less than 43 mg/dL and a systolic BP of more than 115 mm Hg. (In lower-risk patients, serum-creatinine level dropped out as a risk determinant.) The analysis also created three categories of patients with intermediate risk based on various combinations of the three measures.

By 30 days after hospitalization, the readmission rate ran threefold higher in the highest-risk patients, compared with those at the lowest risk.

The new study run by Dr. Win and his associates evaluated how this risk-assessment tool developed to predict in-hospital mortality performed for predicting event rates among community-based heart failure patients who had a total of 5,918 hospitalizations for acute decompensated heart failure at the Mayo Clinic during 2000-2013. They averaged 78 years old, half were women, and 48% had heart failure with preserved ejection fraction.

The risk-level distribution of the 3,628 Mayo patients closely matched the pattern seen in the original ADHERE registry: 63% were low risk, 17% were at intermediate level 3 (the lowest risk level in the intermediate range), 13% were at intermediate level 2, 5% at intermediate level 1, and 2% were categorized as high risk.

For 30-day mortality post hospitalization, patients at the highest risk level had a mortality rate eightfold higher than did the lowest-risk patients, those rated intermediate level 1 had a fivefold higher mortality rate, intermediate level 2 patients had a threefold higher rate, and those at intermediate 3 had a 50% higher rate, Dr. Win reported.

During the 90 days after discharge, mortality rates relative to the lowest risk level ranged from a sixfold higher rate among the highest-risk patients to a 50% higher rate among patients with an intermediate 3 designation.

Analysis of rehospitalizations for heart failure showed that, by 30 days after hospitalization, the readmission rate ran threefold higher in the highest-risk patients, compared with those at the lowest risk and fourfold higher among those at intermediate risk level 1.

Heart failure readmissions by 90 days following the index hospitalization ran threefold higher for both the highest-risk patients as well as those at intermediate level 1, compared with the patients at lowest risk.

The new analyses also showed that roughly similar risk patterns occurred regardless of whether patients had heart failure with reduced or preserved ejection fraction during their index hospitalization, although the relatively increased rate of 30-day mortality with a worse risk profile was most dramatic among patients with reduced ejection fraction. Age, sex, and comorbidity severity did not have a marked effect on the relationships between event rates and risk levels, Dr. Win said.

Dr. Win had no disclosures.

mzoler@frontlinemedcom.com
On Twitter @mitchelzoler

Risk stratification of hospitalized heart failure patients

Risk level	BUN	Systolic BP	Serum creatinine
High	≥43 mg/dL	<115 mm Hg	≥2.75 mg/dL
Intermediate 1	≥43 mg/dL	<115 mm Hg	<2.75 mg/dL
Intermediate 2	≥43 mg/dL	≥115 mm Hg	NA
Intermediate 3	<43 mg/dL	<115 mm Hg	NA
Low	<43 mg/dL	≥115 mm Hg	NA

Note: Based on data from 65,275 patients in the Acute Decompensated Heart Failure National Registry.

Source: JAMA 2005 Feb 2;293(5):572-80

FRONTLINE MEDICAL NEWS

FDA finds clopidogrel does not boost cancer, death

BY JENNIE SMITH
Frontline Medical News

Long-term use of the blood-thinning agent clopidogrel did not alter the risk of death in people with heart disease or at risk of developing heart disease, nor did the drug appear to affect cancer risk, according to a statement from the U.S. Food and Drug Administration.

The FDA's meta-analysis looked at results from 12 trials enrolling a total of 56,799 patients to evaluate the effect of long-term clopidogrel use on all-cause mortality. The incidence of all-cause mortality was 6.7% for the long-term clopidogrel plus aspirin arm and 6.6% for the comparator, resulting in a Mantel Haenszel Risk Difference (MH RD) of 0.04% (95% confidence interval, –0.35%-0.44%).

"The results indicate that long-term (12 months or longer) dual-antiplatelet therapy with clopidogrel and aspirin do not appear to change the overall risk of death, compared with short-term (6 months or less) clopidogrel and aspirin, or aspirin alone," the agency said in its statement.

FDA NEWS

The FDA also conducted a meta-analysis looking at nine of these trials (n = 45,374) that had enrolled patients with coronary artery disease or patients at risk of CAD. This also suggested no difference in the risk of all-cause mortality (MH RD –0.07%; 95% CI, –0.43%- 0.29%).

The meta-analysis included results from the Dual-Antiplatelet Therapy Trial (DAPT), whose results included a worrisome safety signal for extended use of clopidogrel (N Engl J Med 2014; 371:2155-66). Patients in the DAPT underwent percutaneous coronary intervention and placement of a drug-eluting stent, after which they received 1 year of clopidogrel or prasugrel plus aspirin. About 1,000 patients were then randomized to 18 additional months of one of the dual-antiplatelet therapies or to aspirin plus placebo. Extended (30-month) use of clopidogrel plus aspirin was associated with a significantly increased risk of death (2.2% for 30 months vs. 1.5% for 12 months), whereas no increased risk was seen for prasugrel plus aspirin. A higher risk of death was mainly due to noncardiovascular causes, including cancer and trauma.

The DAPT did not show an increased risk of cancer-related adverse events related to treatment duration. However, the FDA performed two meta-analyses of other trials, with about 40,000 patients included in each analysis, to determine whether a signal could be found for either cancer-related adverse events or cancer-related death. Neither revealed an increased risk related to long-term clopidogrel use.

NOW APPROVED

Nucala®
(mepolizumab)
for Subcutaneous Injection
100 mg/vial

Visit **NUCALAinfo.com**
for additional information,
including full Prescribing Information.

www.GSKSource.com

 Printed in USA. 424636R0 October 2015

Alectinib approved for metastatic ALK-positive NSCLC

BY DENISE FULTON
Frontline Medical News

Alectinib has been approved by the Food and Drug Administration for the treatment of patients with metastatic ALK-positive non–small cell lung cancer (NSCLC) who have been treated unsuccessfully with crizotinib.

Alectinib was approved based on data from two single-arm clinical trials of patients with crizotinib-refractory metastatic ALK-positive NSCLC.

One study, conducted in North America, included 87 patients who were treated with 600 mg of oral alectinib twice daily. A total of 38% of patients experienced a reduction in tumor size with a 7.5-month duration of response. In the second trial with the same treatment regimen, conducted globally, 44% of patients saw a reduction in tumor size with an 11.2-month duration of response.

Treatment with alectinib also reduced the size of brain metastases in 61% of patients in a pooled subset of patients in both trials, with a 9.1-month duration of response.

Alectinib will be marketed as Alecensa by Genentech.

dfulton@frontlinemedcom.com

VIEW ON THE NEWS

Dr. Jennifer Cox, FCCP, comments: ALK-positive NSCLC patients who have become refractory to crizotinib now have another treatment option. Alectinib has been approved for use in ALK-positive patients who no longer respond to crizotinib therapy. Duration of response was 7.5 months in North America and 11.2 months globally. In the majority of patients with brain metastases, there was a significant reduction in size of the metastases with a 9.1 month duration of response. Continued development of lung cancer treatment drugs that can extend the length and quality of life is a must.

Pneumonitis requires withholding checkpoint inhibitors

BY NEIL OSTERWEIL
Frontline Medical News

BOSTON – Treatment of pneumonitis associated with the PD-1 axis checkpoint inhibitors requires close monitoring of patients and rapid clinical response, an oncologist advised.

"We need to be vigilant when we treat our patients. If a patient has cough or shortness of breath, you take it seriously, even if [it is] a patient who has lung cancer and is a smoker," said Dr. Scott Gettinger of Yale Cancer Center, New Haven, Conn.

He recommended that before starting patients on a programmed death-1 (PD-1) axis inhibitor such as pembrolizumab (Keytruda) or nivolumab (Opdivo), clinicians get baseline oxygen saturation levels to obtain an objective measure for following patients during therapy.

"When you suspect pneumonitis you have to start steroids right away, or patients can spiral down," he said at the AACR/NCI/EORTC International Conference on Molecular Targets and Cancer Therapeutics.

Pneumonitis – characterized by cough, dyspnea, and hypoxia – is a common adverse event associated with PD-1 and PD-ligand 1 (PD-L1) inhibitors, but is rarely seen in patients treated with CTLA-4 inhibitors such as ipilimumab (Yervoy).

Current evidence suggests that pneumonitis is more prevalent in patients with non–small-cell lung cancer, occurring in approximately 4%-6% of patients cases, than in melanoma (1%). The difference is probably due to a history of smoking common to the majority of patients with NSCLC, Dr. Gettinger said.

"The other theme that we're beginning to see is that maybe pneumonitis is a bit more common with anti-PD-1 vs. anti-PD-L1 antibodies," he said.

It's theorized that PD-1 inhibitors may block binding of PD-L2 to one of its binding partners, thereby interfering with respiratory tolerance, he said.

Evidence from the pivotal clinical trial of nivolumab in lung cancer (Checkmate 057) suggests that the time to onset of pneumonitis was a median of 31.1 weeks (range 11.7 to 56.9 weeks). The pneumonitis resolved in about 5-7 weeks.

Investigators at Memorial Sloan Kettering Cancer Center in New York City reported at the European Cancer Congress 2015 on pneumonitis in 36 of 653 patients treated with an anti PD-1/PD-L1 monoclonal antibody from 2009 through 2014, 33 of whom had received a PD-1 inhibitor, and 3 of whom received a PD-L1 inhibitor.

They found that pneumonitis in patients with lung cancer tended to resemble chronic obstructive pneumonia, whereas patients with melanoma were more likely to have ground-glass opacifications on radiography. There was a trend, falling just short of significance, toward association of COP-like pneumonitis with development of grade 3 or greater, and with a requirement for more than one type of immunosuppression, compared to other subtypes.

Algorithms for management

Dr. Gettinger briefly outlined an algorithm offered by Bristol-Myers Squibb for management of suspected pulmonary toxicity with nivolumab.

For management of patients with grade 1 toxicities (asymptomatic, radiographic changes only), it recommends that clinicians consider delay of immuno-oncologic (I-O) therapy, monitor for symptoms every 2-3 days, and consider consultations with pulmonary and infectious disease specialists.

For grade 2 pneumonitis, marked by mild to moderate new symptoms, the algorithm calls for clinicians to delay I-O therapy per protocol, consult with pulmonary and ID specialists, monitor symptoms daily and consider hospitalization, start the patient on steroids with 1.0 mg/kg per day methylprednisolone IV or the oral equivalent, and consider bronchoscopy and lung biopsy.

For patients with grade 3 or 4 toxicities, marked by severe new symptoms, new or worsening hypoxia, or other life-threatening symptoms, the algorithm states that clinicians should discontinue I-O therapy, hospitalize the patient, consult with pulmonary and ID, give 2-4 mg/kg per day methylprednisolone IV or the oral equivalent, add prophylactic antibiotics for opportunistic infections, and consider bronchoscopy and lung biopsy.

At Yale, Dr. Gettinger and colleagues, when presented with a symptomatic patient on a PD-axis inhibitor, will first rule out other etiologies such as infection, chronic obstructive pulmonary disease exacerbation, or cancer progression), typically with bronchoscopy. For patients with moderate pneumonitis, they may treat with prednisone for 1 or 2 weeks, with a 4-6 week taper begun as symptoms start to resolve.

"In a patient who has profound hypoxia and shortness of breath, we may want to go higher: We might give them 2 mg/kg twice a day of [methylprednisolone] in the hospital, wait until they get better, and then slowly taper them, whether it be over 4 or 6 weeks or longer. Occasionally our patients need to get even higher doses of steroids and there's really nothing to guide us. Who knows if 1 gram of [methylprednisolone] may be better than 60 g of prednisone? But we do it, and patients do get better with the higher doses," he said.

In rare instances, patients may required other immunosuppressive agents, such as infliximab (Remicade), cyclophosphamide, or mycophenolate mofetil.

Patients who require additional immunosuppressive agents to resolve severe pneumonitis tend to have poor outcomes, Dr. Gettinger said.

Re-challenge of patients with a PD-1 or PD-L1 inhibitor following resolution of pneumonitis appears to be inadvisable for all patients except possibly those with grade 1 (asymptomatic) toxicity, due to the high risk of recurrence, he said.

VIEW ON THE NEWS

Dr. Jennifer Cox, FCCP, comments: Baseline oxygen saturations should be obtained on patients when considering or initiating therapy with anti-PD-1 or anti-PDL-1 immuno-oncologics, which are used in both NSCLC and melanoma treatment. Pneumonitis, a common and potentially fatal toxicity seen with these medications, is more common in NSCLC than in melanoma and with the anti-PD-1 than the anti-PDL-1 immunologics. Early symptoms can often be overlooked or trivialized by patients. Cough, shortness of breath or development of hypoxia should prompt an early and aggressive approach to rule out pneumonitis. Initiation of treatment with steroids is a must if there is suspicion of pneumonitis. Hospitalization may be necessary and treatment with additional immunosuppressants needed. Delaying or ceasing further therapy is part of the treatment algorithm depending on severity of symptoms. Having taken care of this population of patients, I can attest that if left unchecked, they can rapidly deteriorate into acute respiratory failure and death.

ZYFLO connect®

Savings. Shipping. Support.

$0 monthly co-pay*
up to $2,500 per month in savings on every prescription

FREE next-day delivery
direct to your patient's door

Reimbursement support
by phone to help with the PA process if required

Pharmacist on call 24/7
to answer questions

Refill reminder phone calls
from a ZYFLO Connect pharmacist

Simple and streamlined
enrollment process via phone, fax, or EMR

CONNECT patients with VALUABLE BENEFITS

Contact your patients about these benefits today

Visit myZYFLO.com or **Call 1-844-ZYFLO-RX**

*Terms and conditions apply. Please see full Terms and Conditions on adjacent page.

Chiesi

ZYFLO connect®

Savings. Shipping. Support.

ZYFLO CONNECT® PROGRAM – TERMS & CONDITIONS

HOW IT WORKS

If you are uninsured or have commercial insurance, including insurance purchased through the Affordable Care Act Exchange plans, Chiesi USA may help pay the out-of-pocket expenses (co-pay, co-insurance, deductibles) of your prescription. For patients taking ZYFLO CR® (zileuton) extended-release tablets, up to $2,500 per month will be provided, if you meet the eligibility requirements below. If the total costs of your out-of-pocket expenses are over $2,500 per month, you will be responsible for the outstanding balance.

ELIGIBILITY REQUIREMENTS

- You are either:
  - Uninsured, or
  - You are insured by commercial or private insurance and your insurance does not cover the full cost of ZYFLO CR
- Your prescriptions are not covered in full or in part by any state or federally funded insurance program, including but not limited to Medicare, Medicaid, Medigap, Veterans Affairs (VA) or Department of Defense (DOD) programs, or the Government Health Insurance Plan available in Puerto Rico (formerly known as "La Reforma de Salud"); patients who move from commercial to state or federally funded prescription insurance will no longer be eligible
- You are at least 18 years of age
- Void where prohibited by law

TERMS OF USE

- By accepting this offer and participating in the ZYFLO Connect program, you are representing and warranting to Chiesi that you currently meet the eligibility requirements described above and will comply with these Terms of Use.
- Out-of-pocket benefit equals an amount up to $2,500 per month (maximum benefit of $30,000 per year) for ZYFLO CR. Patient is responsible for applicable taxes, if any.

  EXAMPLE: If your monthly ZYFLO CR prescription co-pay or out-of-pocket cost is $3,000, eligible patients will only pay $500 per month for ZYFLO CR, a savings of $2,500 off of their co-pay or total out-of-pocket costs. If your co-pay or out-of-pocket costs are no more than $2,500, you pay $0. For a mail-order 3-month prescription, your total maximum savings will be $7,500 ($2,500 x 3).
- If a patient exceeds the maximum monthly benefit of $2,500, the patient will be responsible for the outstanding balance.
- Patients, pharmacists, and prescribers cannot seek reimbursement from health insurance or any third party, for any part of the benefit received by the patient through this offer.
- Your acceptance of this offer confirms that this offer is consistent with your insurance and that you will report the value received as may be required by your insurance provider.
- Only valid in the United States or Puerto Rico; this offer is void where restricted or prohibited by law.
- No membership fees.
- The ZYFLO Connect program is not insurance.
- The ZYFLO Connect program cannot be combined with any other rebate/coupon, free trial, or similar offer for the specified prescription.
- The ZYFLO Connect program expires on December 31, 2016.
- The ZYFLO Connect program is limited to one per person.
- Chiesi USA reserves the right to rescind, revoke, or amend this offer at any time without notice.
- **The ZYFLO Connect program is only offered through distribution from Foundation Care, a full-service pharmacy serving patients in all 50 states and Puerto Rico.**

  Foundation Care, 4010 Wedgeway Court, Earth City, MO 63045 Phone: (844) 699-9356

Chiesi

ZYFLO CR®
(zileuton) extended-release tablets

PULMONARY PERSPECTIVES: Surgery for pulmonary NTM infections

BY DR. JOHN D. MITCHELL, FCCP

Although recognized with increasing frequency in the United States, the treatment of pulmonary infection related to nontuberculous mycobacteria (NTM) can admittedly be difficult. The recommended drug regimen (when prescribed correctly) is arduous and prolonged and may be complicated by drug intolerance, toxicity, or resistance. Patients may experience repeated recurrence of the infection, often associated with progressive symptoms and dwindling therapeutic options.


DR. MITCHELL

This scenario is particularly common with so-called "rapid-grower" infections, such as *Mycobacterium abscessus*, leading to failure of conventional treatment. In these situations, the use of surgical resection has been proposed as an adjunct to medical therapy to improve outcomes in this patient population. The rationale for adding surgery to the treatment of affected patients is that the areas of parenchymal disease are poorly penetrated by the antibiotic therapy, thus, serving as a reservoir for organisms to trigger recurrent infection. In this article, we explore the use of surgery in patients with pulmonary NTM infection.

Surgery must be seen as an adjunct to, and not a replacement for, conventional medical treatment, which remains the mainstay of therapy and should be continued for several months after successful surgical intervention.

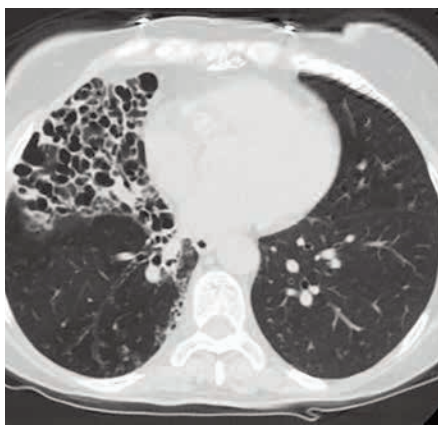


Figure 1. CT scan image demonstrating right middle lobe bronchiectasis associated with NTM infection, amenable to VATS resection.

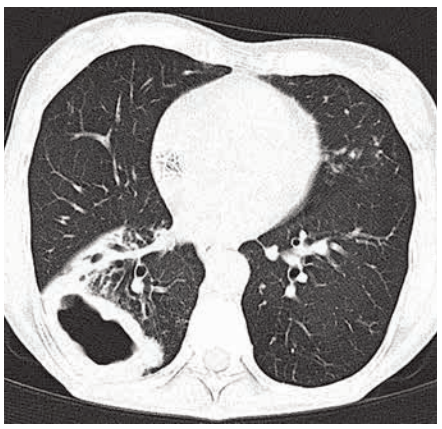


Figure 2. CT scan image demonstrating right lower lobe cavitary disease associated with NTM infection. Despite the cavity size, the thick walled nature of the cavity and the focal juxtaposition to the parietal pleura render it amenable to VATS resection.

Initial considerations

At the outset, several points about the use of surgical resection in this patient group should be emphasized. First, the use of surgery must be seen as an adjunct to, and not a replacement for, conventional medical treatment. The appropriate drug regimen remains the mainstay of therapy and should be continued for several months after (apparently) successful surgical intervention. This fact is often lost on patients undergoing therapy for years with recurrent treatment failure. Further, one should recognize that not all patients are candidates for surgery; in our program, only a small proportion of evaluated pulmonary patients with NTM infection are considered for surgical intervention. Individuals invariably describe a pattern of recurrent infections, usually in the setting of significant drug intolerance or resistance. In addition, they must possess focal parenchymal damage – typically end-stage bronchiectasis or persistent cavitary lung disease – to serve as surgical "targets" for removal. Finally, the decision for surgical intervention is best made in a multidisciplinary setting, carefully weighing all treatment alternatives. At our institution, all prospective candidates for surgery are discussed in detail within our multidisciplinary group, including the timing and extent of surgical resection and the use of other procedures, such as muscle flap transposition. We strongly feel this improves patient outcomes.

What is the goal?

When considering surgery in patients with NTM infection, it is important to identify the goals of the proposed operative intervention. What do we hope to accomplish by operating on this patient? In most cases, the goal is to eradicate the infection – render the patient culture-negative, off antibiotic therapy. Unfortunately, this is not possible in all cases due to the extent of the parenchymal disease. However, we have found surgery may be helpful in two additional situations. First, the presence of disabling or life-threatening symptoms, such as intractable cough or significant hemoptysis, may be alleviated with surgical intervention. Second, in some patients, surgery may be able to slow down or even halt the progression of the disease by "debulking" or removing large areas of significant parenchymal damage. These areas, if left in situ, can soil uninvolved areas of lung parenchyma. An example of this would be the patient with a cavitated, completely destroyed lung and limited disease in the contralateral lung; removal of the destroyed side will limit ongoing contamination to the remaining lung.

Continued on following page

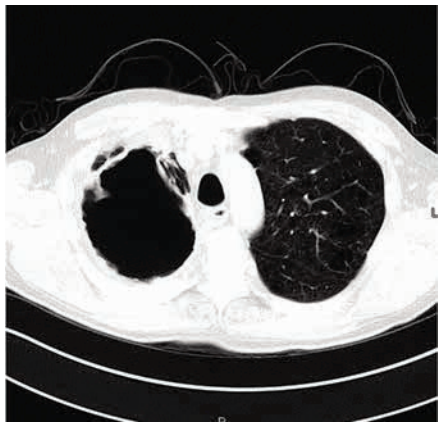


Figure 3. CT scan image demonstrating a destroyed right upper lobe associated with NTM infection. This thin-walled cavity requires an open, extrapleural approach for safe excision.

Preparation for surgery

The timing of surgical intervention is important. At our institution, the medical regimen is optimized with the collection of new cultures and drug susceptibility testing, when appropriate. Surgery is usually planned 8-12 weeks later, at a time when the mycobacterial counts could be anticipated to be at a low point.

Occasionally, the final decision regarding the extent of surgical re-

Continued from previous page

section may hinge on updated imaging after initiation of the improved regimen.

Factors that may alter this traditional approach include the presence of an adequate medical regimen on presentation, which may accelerate the path to surgery; or a poorly controlled infection, heavy burden of disease, or poor nutritional status, which may slow the path to surgery.

Of course, patients must be acceptable candidates for surgical resection in the traditional sense – adequate pulmonary reserve and a general lack of disqualifying medical comorbidities.

Interestingly, what constitutes "adequate pulmonary reserve" in this patient cohort often differs from the typical thoracic patient undergoing surgery for cancer.

In pulmonary NTM infection, the targets of surgical resection, because of significant cavitary disease or bronchiectasis, have very little function and, thus, may cause little decrement in the patient's pulmonary status once removed. Thus, in the absence of other mitigating factors, a patient with NTM infection with borderline function (for example, forced expiratory volume in 1 second = 35%), and a destroyed left lung remains a candidate for pneumonectomy.

Surgical approach

An open thoracotomy approach has traditionally been used in patients with bronchiectasis and cavitary lung disease, producing excellent results with acceptable morbidity and mortality in several published studies. Within the past decade, though, it has become increasingly clear that many (if not most) of these operations may be accomplished through a minimally invasive, or VATS [video-assisted thoracoscopic surgery] approach.

The key, as with so many surgical techniques, lies with proper patient selection. Figures 1 to 3 (see page 13) depict examples of the parenchymal disease of patients with NTM infection and the surgical approach used. The degree of pleural symphysis and the extent of cavitary lung disease on the CT scan images are the crucial elements to assess deciding if a VATS approach is feasible.

We favor anatomic lung resection whenever possible in this patient population, believing that this produces the best clearance of diseased parenchyma. However, lobectomy or segmentectomy for bronchiectasis or cavitary lung disease poses several technical challenges when compared with a similar procedure for thoracic malignancy. Pleural adhesions are almost always present to some degree, and, in some cases, can be extensive and vascular in nature. They usually involve the affected segment(s) of lung but can also be scattered throughout the hemithorax.

In cavitary upper lobe disease, the adhesions to the overlying parietal pleura can be significant. In almost all cases, the adhesions can be divided through a minimally invasive approach, often with improved visibility compared with thoracotomy.

Indications to convert to an open approach would include the perceived need for an extrapleural dissection or because of concern regarding underlying vital structures. As noted previously, CT scanning will usually predict the presence of dense adhesions but may underestimate the amount of pleural symphysis.

Further technical obstacles include a hypertrophied bronchial circulation and considerable lymphadenopathy may be present within the ipsilateral hilum. Although a nodal dissection is clearly not required, the lymphadenopathy in the setting of chronic pulmonary granulomatous disease can make dissection of the hilar vessels difficult. Additionally, the diseased lung tissue is thickened and tends to compress poorly, thus making it a poor substrate for staple closure. Routine buttressing of the bronchial stump to prevent bronchopleural fistula is unnecessary in this group of patients; situations in which buttressing of the bronchial stump should be considered would be in the presence of a multidrug-resistant organism, in the setting of poorly controlled infection before surgery, or after pneumonectomy. Finally, it should be understood that surgical success in this patient population can be difficult to come by, and as with so many other endeavors, experience counts.

In pulmonary NTM infection, the targets of surgical resection, because of significant cavitary disease or bronchiectasis, have very little function and, thus, may cause little decrement in the patient's pulmonary status once removed.

Outcomes

Our institution has enjoyed considerable success in the use of surgery in select patients with pulmonary NTM infection. In addition, several other retrospective studies have demonstrated excellent results following surgery for pulmonary NTM disease, with very low morbidity and mortality and high sputum conversion rates. Understandably, there is considerable bias in these reports involving select patient populations, and, in general, there are limited data regarding patient selection and long-term outcomes in this field. Clearly, further research is needed.

Dr. Mitchell is the Courtenay C. and Lucy Patten Davis Endowed Chair in Thoracic Surgery; professor and chief, section of general thoracic surgery, division of cardiothoracic surgery, University of Colorado School of Medicine; and National Jewish Health, both in Aurora.

Bibliography

Griffith DE, et al. An official ATS/ISDA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med*. 2007;175:367.
Mitchell JD, et al. Anatomic lung resection for nontuberculous mycobacterial disease. *Ann Thorac Surg*. 2008;85:1887.
Mitchell JD, et al. Thoracoscopic lobectomy and segmentectomy for infectious lung disease. *Ann Thorac Surg*. 2012;93:1033.
Shiraishi Y, et al. Different morbidity after pneumonectomy: multidrug-resistant tuberculosis versus non-tuberculous mycobacterial infection. *Interact Cardiovasc Thorac Surg*. 2010;11:429.
Shiraishi Y, et al. Adjuvant surgical treatment of nontuberculous mycobacterial lung disease. *Ann Thorac Surg*. 2013;96:287.
Watanabe M, et al. Early pulmonary resection for *Mycobacterium avium* complex lung disease treated with macrolides and quinolones. *Ann Thorac Surg*. 2006;81:2026.
Yu JA, et al. Lady Windermere revisited: treatment with thoracoscopic lobectomy/segmentectomy for right middle lobe and lingular bronchiectasis associated with nontuberculous mycobacterial disease. *Eur J Cardiothorac Surg*. 201;40:671.

New Section Editor for Pulmonary Perspectives

We welcome Dr. Nitin Puri, FCCP, as our new Section Editor for Pulmonary Perspectives. He is an Assistant Professor of Medicine at Cooper Medical School of Rowan University, Camden, N.J. He did his Internal Medicine training at Grady Hospital in Atlanta at Morehouse School of Medicine and his Pulmonary Medicine and Critical Care Medicine training was done at Cooper Hospital. He is the Associate Program Director for Critical Care Medicine and was previously Director of the Cardiac Surgery ICU at Inova Fairfax, Falls Church, Virginia. Dr. Puri's special interests include quality improvement, bedside ultrasound, and mechanical circulatory support.

DR. PURI

Spirometry identifies risk in asymptomatic adults

BY MITCHEL L. ZOLER
Frontline Medical News

ORLANDO – Unselected people from the general population without clinically apparent lung disease but with low lung function had significantly increased mortality during follow-up that was independent of cardiac function, in results from more than 13,000 middle-aged Germans.

"Subtle, subclinical pulmonary impairment is a risk indicator for increased mortality independent of cardiac performance," Dr. Christina Baum said at the American Heart Association scientific sessions.

The researchers used spirometry to measure each subject's forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC). The results showed that "spirometry is a good screening tool that is not very expensive," making spirometry an effective risk assessment tool for use in the general adult population, said Dr. Baum of the department of general and interventional cardiology at the University Heart Center in Hamburg, Germany.

She and her associates used data collected in the Gutenberg Health Study, which enrolled more than 15,000 German women and men aged 35-74 years during 2007-2012. The investigators excluded people with a history of pulmonary disease, resulting in a study cohort of 13,191, who averaged 55 years old, with 51% men.

At enrollment into the study, all people underwent screening spirometry and echocardiography. Their average baseline FEV_1 was 2.9 L and their average FVC was 3.7 L, and 4% had heart failure based on assessments of left ventricular size and function by echocardiography.

The first 5,000 enrollees also had measurements taken of their serum levels of *N*-terminal probrain natriuretic peptide and cardiac troponin I through use of a high-sensitivity assay. The researchers used data from patients followed for a median of 5.5 years.

During follow-up, people in the lowest tertile for FEV_1 and those in the lowest tertile for FVC had higher rates of all-cause mortality, compared with those in the highest tertile for each of these two parameters.

In a multivariate analysis that adjusted for age, sex, body mass index, smoking status, hypertension, dyslipidemia, heart failure status, serum levels of *N*-terminal probrain natriuretic peptide and cardiac troponin I, and other parameters, people with lower FEV_1 and FVC readings had significantly worse survival, Dr. Baum said.

Every 1–standard deviation increase in FEV_1 was linked with a statistically significant, 38% reduced mortality rate; furthermore, a similar significant inverse association existed between FVC and mortality, she reported.

mzoler@frontlinemedcom.com
On Twitter @mitchelzoler

INTRODUCING

CO-SUSPENSION TECHNOLOGY

THE NEW SCIENCE OF INTELLIGENT DELIVERY IN RESPIRATORY MEDICINE

Exploring a new formulation for inhaled drug delivery

A specially engineered, phospholipid carrier particle with multiple drug crystals[1]

Visit Co-SuspensionParticles.com
to Learn More

CO-SUSPENSION
TECHNOLOGY

All images are for illustrative purposes only.

Reference: 1. Vehring R, Lechuga-Ballesteros D, Joshi V, Noga B, Dwivedi SK. Cosuspensions of microcrystals and engineered microparticles for uniform and efficient delivery of respiratory therapeutics from pressurized metered dose inhalers. *Langmuir*. 2012;28(42):15015-15023.

AstraZeneca

SLEEP STRATEGIES: Lesser known eye complications of OSA

BY DR. SUNITA KUMAR, FCCP; AND DR. FARBOD GHODS

It is estimated that there are 25 million people with obstructive sleep apnea (OSA) in the United States, of whom 82% remain undiagnosed. The prevalence of the condition ranges from 4% to 9%, and prevalence runs higher in those with obesity. OSA is associated with significant morbidity related to its cardiovascular and metabolic consequences including, but not limited to, increased risk of coronary artery disease, arrhythmias, diabetes, stroke, and all-cause mortality. While most sleep specialists are familiar with the aforementioned adverse effects, many are unaware of OSA's lesser known effects on the eye and its association with nocturia, which will be discussed here.

Floppy eyelid syndrome (FES) was one of the first recognized ocular complications of OSA. FES is caused by a weak tarsal plate, which is commonly seen in obese and older patients, as well as those with sleep apnea. The condition is characterized by easy eversion of the upper eyelids with minimal lateral traction and is associated with papillary conjunctivitis of the upper palpebral conjunctiva. Multiple pathogenic mechanisms have been postulated for FES. The extracellular matrix of the eyelids with FES shows a significant decrease in mature elastic fibers and an increase in oxytalan fibers. The altered elastic fiber phenotype with collagen accumulation was considered part of an adaptive response to recurrent mechanical loading of the tarsal plate. In 1999, Mojan et al studied a cohort of 72 patients with suspected OSA and found FES in 32% of patients with OSA compared with only 3.6% of those without OSA (*Ophthalmology*. 1999;106[6]:1182). Later, Ezra

DR. KUMAR

DR. GHODS

et al reported significant association between FES and OSA, keratoconus, and lash ptosis (*Ophthalmology*. 2010;117[4]:831). A recent study of veterans attending a geriatrics clinic showed that 55% had eyelid laxity, and the risk was higher with older age, higher body mass index, and a diagnosis of sleep apnea (Ansari et al. *Cornea*. 2015;34[1]:32). Diagnosis of FES is based on ocular signs, including easy or spontaneous eversion of the upper eyelids in conjunction with conjunctivitis and keratitis. This condition should be suspected in any obese patient with a chronic red and tearing eye. Treatment consists of conservative measures, such as lubrication ocular drops and ointments, eyelid taping, or a night eye shield. Multiple surgical techniques to address horizontal laxity and redundant eyelid tissues have been attempted with various success. However, in patients with FES and OSA using CPAP, poor mask fitting (a poor seal between the device and the facial tissues) can aggravate the condition causing exposure keratoconjunctivitis from the air leaking around the mask. Refitting of the masks can be helpful in such situations (Pham et al. *Curr Opin Ophthalmol*. 2007;18[5]:430).

Non-arteritic anterior ischemic optic neuropathy (NAION) is the second most common optic neuropathy in adults. Annual incidence in the United States is 2.3 to 10.2 per 100,000 population. It presents with loss of vision over hours to days, usually with blurring and dimness. Prevalence of OSA has been reported as 71% to 89% in case series of patients with NAION (Polombi et al. *Br J Ophthalmol*. 2006; 90[7]:879). Investigation into the link between NAION and sleep apnea was prompted by the classic presentation of acute painless vision loss upon awakening in the morning in nearly 75% of patients with NAION. Different mechanisms have been suggested, including an acute or subacute ischemia of the head of the optic nerve. These ischemic events can be due to fluctuation in blood flow because of variations in blood pressure and increases of intraocular pressure, as well as hypoxic episodes that occur during obstructive respiratory events. Although it is not possible to reverse vision loss from NAION, treatment of sleep apnea may help prevent an attack of NAION in the other eye, which occurs in 15% to 18% of cases. In a prospective follow-up of 118 patients with NAION, 75% of whom had OSA, Aptel et al found that the risk of occurrence of NAION in the other eye increased with nonadherence to CPAP therapy (Aptel et al. *JAMA Ophthalmol*. 2015;133[7]:797).

Glaucoma: Prevalence of OSA in patients with primary open angle glaucoma (POAG) and normal tension glaucoma (NTG) has been reported to range from 20% to 57%. Conversely, the prevalence of glaucoma in OSA patients ranges from 2% to 27%. Intraocular pressure (IOP)-independent mechanisms stemming from episodic hypoxia may be the link between OSA and glaucoma. Blood pressure fluctuations seen with obstructive respiratory events may affect perfusion pressure of the optic nerve head causing ischemia, oxidative stress, and inflammation. These mechanisms are similar to those associated with NAION. Other possible mechanisms postulated include disrupted autoregulation of blood flow to the optic nerve from hypoxia and hypercapnia; episodic arterial hypertension from repetitive sympathetic activation during arousal; hypercapnia-induced cerebral vasodilation leading to increased intracranial pressure; and catecholamine-induced platelet activation (Faridi et al. *Clin Experiment Ophthalmol*. 2012;40[4]:408). Some recent studies, however, have disputed the association of glaucoma with OSA. A French study, using a large prospective clinical cohort, showed similar prevalence of glaucoma in patients with and without OSA (Aptel et al. *Sleep Medicine*. 2014;15[5]:576). Similarly, another large retrospective cohort study using insurance-claims database did not find an increased risk of glaucoma among patients with OSA (Stein et al. *Am J Ophthalmol*. 2011;152[6]: 989).

Retinal vein occlusion (RVO) has been more recently associated with OSA. In a study of 63 consecutive patients with RVO, Glacet-Bernard et al identified 30 with positive risk factors for OSA, of whom 77% had OSA. They postulated that the association of RVO and OSA could be related to slowing down of blood circulation due to hypoxemia and elevated nocturnal ICP. In a study from Taiwan, the risk of incident RVO was 1.94 times higher in patients with a diagnosis of OSA compared with a matched cohort of patients without OSA (Chou et al. *Am J Ophthalmol*. 2012;154[1]:200).

Although it is not possible to reverse vision loss from NAION, treatment of sleep apnea may help prevent an attack of NAION in the other eye, which occurs in 15% to 18% of cases.

Nocturia is defined as two or more episodes of waking up to void during a sleep period. Its prevalence increases with age, ranging from 9% in women to 27% in men younger than 40 years; and 19% in women and 42% in men over the age of 40

Continued on following page

Continued from previous page

(*Curr Urol Rep*. 2015;16[9] 66). It is one of the most disturbing sleep complaints and is independently associated with decreased state of health and increased mortality. Nocturia may occur as a result of polyuria, a urine output of greater than 40 mL per kilogram in a 24-h period. When more than a third of this volume is excreted during the night, it is termed as nocturnal polyuria. It may also be a consequence of decreased bladder storage arising from detrusor over-activity, bladder hypersensitivity, or reduced nocturnal capacity. Sleep

Intraocular pressure-independent mechanisms stemming from episodic hypoxia may be the link between OSA and glaucoma.

disruption from other sleep disorders, such as restless legs syndrome, insomnia, and OSA, may also cause nocturia. It is common for patients to attribute wakefulness to lower urinary tract symptoms and not to sleep-disordered breathing. As a result, they often present to urology clinic.

There are several studies showing the association between nocturia and OSA. In one such study conducted in a veterans hospital urology clinic, 49% of the patients were identified to be at risk for OSA based on Berlin's questionnaire, of whom 74% had nocturia. Nocturia as a screening tool for presence of OSA was evaluated in a retrospective study of patients presenting to a sleep clinic and showed sensitivity similar to that of snoring - 84.8% for nocturia and 82.6% for snoring. The study found patient-reported nocturia frequency predicted apnea–hypopnea index (OSA severity) above and beyond body mass index, sex, age, and self-reported snoring.

The mechanism of nocturia in association with OSA has been attributed to increased secretion of atrial natriuretic peptide (ANP) due to increased venous return from negative intrathoracic pressure swings created by efforts to open the obstructed airway. Tachycardia and sympathetic nervous system stimulation from arousals create a false-hypervolemic signal, also leading to increased release of ANP.

Use of CPAP to treat OSA has been shown to reduce urine volume and urinary frequency in a Japanese study (Miyauchi et al. *Urology*. 2014;84[4]:892). Similar results were reported by Fitzgerald et al in a retrospective study of patients presenting to the sleep lab (Fitzgerald et al. *AJOG*. 2006;194:1399) where the frequency of nocturia episodes per 8-hour sleep period decreased from 3 episodes (1-21) in the baseline to 0 (0-9) episodes when the same patient was using CPAP titration.

In summary, when treating patients with OSA, we should educate them regarding the associated ocular complications. Early referral to ophthalmology will be beneficial in many cases. Likewise, when treating patients with FES and nocturia, ophthalmologists and urologists, respectively, should consider evaluating their patients for the risk of OSA and/or refer them to a sleep specialist.

Dr. Kumar is Associate Professor of Medicine, and Dr. Ghods is a Fellow, Pulmonary and Critical Care, Loyola University Medical Center, Maywood, IL.

Lifestyle modification program mitigates sleep apnea

BY MATT MAHADY
Frontline Medical News

FROM CHEST

A dietitian-led lifestyle modification program helped cut the severity of obstructive sleep apnea and reduced daytime sleepiness over a 12-month period, Dr. Susanna S. S. Ng reported in Chest.

Dr. Ng and colleagues at the Chinese University of Hong Kong evaluated 104 patients aged 30-80 years with moderate to severe obstructive sleep apnea and a body mass index of at least 25 kg/mg^2. All patients had an apnea-hypopnea index (AHI) of greater than 15. Patients were randomized to receive a dietitian-led lifestyle modification program or usual care for 12 months.

Patients in the lifestyle modification program met with a dietitian weekly for the first 4 months, then monthly for

the rest of the year. They were advised to cut calories by 10%-20% and eat more protein and fiber, meet at least once with an exercise instructor, and engage in 30-minute aerobic exercise sessions 2-3 times per week. Diet advice was adjusted over time as patients lost weight. Patients in the control arm received lifestyle advice at baseline and at 6 months into the study.

Patients in the lifestyle modification arm lost an average of 1.8 kg; their AHI scores dropped by 17% and BMI dropped 6%. Control patients lost 0.6 kg, their AHI scores increased 0.6%, and their BMI declined by 2% (Chest 2015;148[5]:1193-1203).

Changes in AHI correlated with changes in weight. AHI, first measured 4 months after the initial intensive diet counseling session, was maintained at 12-month follow-up assessment, with no rebound even after the intensive phase of the dietary intervention ended at 4 months. Reduction in daytime sleepiness and a modest improvement in mental health were seen in patients in the lifestyle modification group.

See related commentary on page 22

"Weight reduction should be the core element in the treatment of OSA," the researchers concluded.

VIEW ON THE NEWS

Dr. Octavian C. Ioachimescu, FCCP, comments: Obesity is likely the most important risk factor for obstructive sleep apnea (OSA) in adults. Analyses of the Wisconsin Sleep Cohort Study showed that a weight gain of 10% was associated with an increase in apnea hypopnea index (AHI) of 32%, while a 10% weight loss corresponded to a 26% reduction in AHI. Continuous positive airway pressure (CPAP) is generally the first line of therapy for moderate or severe OSA. Unfortunately, suboptimal adherence to CPAP therapy remains one of the factors limiting outcome modification in this condition. Earlier studies found that CPAP therapy may be associated (as expected) with weight loss, but subsequent studies failed to prove this concept. A recent meta-analysis published by

Continued on following page

References: 1. Raghu G et al; on behalf of the ATS, ERS, JRS, and ALAT. *Am J Respir Crit Care Med*. 2015;192(2):238-248. **2.** OFEV® (nintedanib) Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2014. **3.** Zappala CJ et al. *Eur Respir J*. 2010;35(4):830-836. **4.** Schmidt SL et al. *Chest*. 2014;145(3):579-585. **5.** du Bois RM et al. *Am J Respir Crit Care Med*. 2011;184(12):1382-1389. **6.** Song JW et al. *Eur Respir J*. 2011;37(2):356-363. **7.** Richeldi L et al; for the INPULSIS Trial Investigators. *N Engl J Med*. 2014;370(22):2071-2082. **8.** Richeldi L et al. *N Engl J Med*. 2011;365(12):1079-1087. **9.** US Food and Drug Administration. http://www.fda.gov/downloads/Regulatory Information/Legislation/FederalFoodDrugandCosmeticActFD-CAct/SignificantAmendmentstothe FDCAct/FDASIA/UCM380724.pdf. Accessed September 1, 2015.

Continued from previous page

Drager L. et al. in Thorax 2015, 70(3): 258-64 suggests that CPAP therapy may even increase weight in patients with OSA. Irrespective of what the final verdict on this issue is, it only makes sense to employ a multi-prong approach, by adding to CPAP therapy counselling and lifestyle interventions promoting weight loss in overweight and obese patients with OSA.

Recently, Susanna S. S. Ng et al. from The Chinese University of Hong Kong [*CHEST* 2015;148(5):1193-1203] reported that an aggressive dietitian-driven lifestyle modification program (LMP) for 12 months could led to improvements in OSA severity and seemed to ameliorate daytime sleepiness. In this prospective parallel group randomized open-label study, 104 patients with moderate or severe OSA received either a dietician-led LMP or usual care for

Continued on following page

Continued from previous page

12 months. The OSA was diagnosed by a home sleep testing device and the term AHI was used for the standard respiratory event index. In the LMP group, patients attended dietary consultation weekly for the first 4 months and then monthly until completion of the program. The initial goal of the intervention was a caloric reduction of 10% to 20% from the baseline diet (or at least a 200-Calorie deficit per day), which was subsequently adjusted based on achieved progress and a target BMI of 23 kg/m^2. Patients in the LMP group were also instructed to eat more fruit and vegetables, and were recommended foods with low-calorie, low-fat content. Additionally, patients were encouraged to see an exercise trainer at least once during the program and to perform 20-30 minutes of aerobic exercise two to three times weekly. In the control group, an average of 0.6 kg/m^2 reduction in BMI was noted over the 12-month interval, which may represent an ascertainment or Hawthorne effect ($p<0.001$ in the intent-to-treat analysis). In the LMP group, over the same 12-month interval, an 1.8 and a 2.2 kg/m^2 reduction in BMI were noted in the intent-to-treat and the treatment-per-protocol analyses, respectively. Not surprisingly, the changes in weight closely correlated with the changes in AHI. As such, those who lost at least 15 kg had seen a reduction in AHI of more than 30%, while those in the 5-15 kg weight loss category had seen an average reduction in AHI of more than 10%. Similarly, at 12 months, the control patients had milder daytime symptoms, i.e. an average Epworth Sleepiness Scale (ESS) score lower by 1 unit (statistically non-significant), while in the LMP group the ESS was 2.5 and 3.5 units lower in the intent-to-treat and treatment-per-protocol analyses, respectively (*P* less than 0.001). Unfortunately, only 41% of the participants in the study agreed to initiate CPAP therapy and the CPAP usage was on average only 4.4 hours per night. Also, the study does not tell us what the impact of the dietary intervention and weight loss would be in patients with moderate or severe OSA who are adherent to the CPAP therapy.

While this study is an important addition to the literature on the therapy of OSA, many questions still remain. What seems to be clearer at this point is the fact that optimal long-term management of moderate or severe OSA should be multidisciplinary in nature and include CPAP therapy and sustained behavioral and dietary interventions in order to improve the quality of the patient's diet, to lose weight and (hopefully) to alter the biologic milieu that represents the pathophysiologic basis of OSA.

INDEX OF ADVERTISERS

PRESIDENT'S REPORT: Are we having fun yet?

BY DR. BARBARA PHILLIPS, FCCP, CHEST PRESIDENT; AND CHAD JACKSON, MS, RRT, SENIOR DIRECTOR OF SIMULATION, E-LEARNING, AND INNOVATION

CHEST 2015 was amazing: more than 7,000 attendees from 70 countries, with 400 educational sessions. Why do so many people go to meetings? Of course, major reasons to go to a conference are to learn, get continuing education credits, or achieve credentialing. But, if that's all we really want to do, we can take an online course or read a journal. People go to meetings, at least in part, to have fun.

And Montréal was fun. It's a gorgeous, European-styled city, with lots to see, a laid-back attitude, amazing food, delightful people, great outdoor activities, and excellent public transportation.

DR. PHILLIPS

But the CHEST meeting itself was fun. The all-attendee reception featured entertainment and great food and drink. The Training and Transitions/NetWork mixer offered a chance to socialize while getting to know people in the CHEST NetWorks. There were all kinds of get-togethers, organized and spontaneous, for people to meet, make friends, and collaborate. And that's fun!

But what truly sets CHEST apart from other meetings is that the CHEST organization unabashedly strives to make learning fun. Ever been to the CHEST Challenge? If so, you understand. Why not make a game of it?

My coauthor, Chad Jackson, presented an interesting session at the meeting where he talked about the evolution of games at CHEST meetings. He argued convincingly that learning is enhanced when it's fun, and he is strongly supported by recent literature.[1-3] For example, in a game of simulated response to cardiac arrhythmias, educational content is integrated into a game so that learning is intrinsic to play, which motivates players and improves engagement.[1] This enables players to practice safe, clinical decision-making.

"Serious games" is a term used to define a game that is specifically designed to improve education and training.[4] CHEST has been an innovator in the area of serious games and gaming for many years. One such example is the well-known CHEST Challenge, created by Dr. William Kelly, FCCP. But, Dr. Kelly and other dedicated volunteer faculty, along with the talented and committed CHEST staff, have created several other gaming opportunities for learners.

"Pulmonary Adventures" is a pulmonary and radiology case-based adventure game that participants play in arcade-style cabinets at the annual meeting and other select College events. There are multiple versions of this particular game, as well, which is loosely based on the Indiana Jones movie theme. There is the original "Pulmonary Adventures" game, a "Temple of Gloom" version, and a soon to be released "Last Gasp Crusade" version of the game. These games are fun, interactive, and engaging for learners to play, which is why they have been so popular at CHEST since 2013.

"Sound Dx" is a case-based ultrasound game that allows users to place the simulated ultrasound probe onto a torso, while it plays a video that corresponds to that physiology and then asks the learners to answer specific questions about the "patient." With 12 different cases in each game, there is no shortage of fun for the learner. The game has now been updated, allowing additional feedback to be provided to the learner based on rationales for the answers to the cases.

"Aspirated" is a fast-paced game based on the essential procedure of removing a small aspirated item from the airway. Learners are challenged to insert an actual bronchoscope into a torso task trainer and recover a small piece of candy or other food item. The twist to the game is that the learner is timed during the retrieval. Timing starts as soon as the scope passes the teeth, and ends when the learner successfully removes the aspirate from the mouth, after successful retrieval. During this past CHEST Annual Meeting, Dr. Majdeline Farah, a local physician from Quebec, Canada, completed the task in a record 25.85 seconds to win an iPad®.

"Whack-a-Doc" is based on COPD cases. Physicians must decide on whether they agree or disagree with the physician's recommendations in the game, and then "whack" the one with whom they disagree on their plan. This game is a fully electromechanical arcade game that has been created by faculty and staff at CHEST.

In their comprehensive review of serious games, Ricciardi and coworkers described the differences between simulations and serious games in four categories defined as entertainment factor, developmental costs, developmental time, and deployment costs.[5] Serious games, while similar to simulation, are distinctly different. They provide more entertainment but lower associated development costs, development time, and deployment costs. This explains why serious games has become so popular as a teaching tool for clinicians.

The winning CHEST Challenge 2015 team, for the second year in a row, is from Cleveland Clinic.

Why has CHEST been successful in creating such fun and interactive serious games? Teamwork between remarkable volunteers and dedicated staff. Why has this innovation been so popular? Serious games are fun for people to play because they can challenge learners while keeping them engaged. Serious gaming is part of how CHEST maintains its place as the global leader in clinical education.

References

1. Kaczmarczyk J, Davidson R, Bryden D, Haselden S, Vivekananda-Schmidt P. Learning decision making through serious games. *Clin Teach.* 2015; Jul 27. Published online first. doi: 10.1111/tct.12426.
2. Diehl LA, de Souza RM, Gordan PA, Esteves RZ, Coelho IC. User assessment of "InsuOnLine," a game to fight clinical inertia in diabetes: A pilot study. *Games Health J.* 2015;4:335-343.
3. Wood SJ, Woywodt A, Pugh M, Sampson I, Madhavi P. Twelve tips to revitalise problem-based learning. *Med Teach.* 2014;17:1-7.
4. Annetta L. The "I's" have it: A framework for serious educational game design. *Rev Gen Psychol.* 2010;14(2):105-112.
5. Ricciardi F, Tommaso De Paolis L. A comprehensive review of serious games in health professions. *Internat J Computer Games Tech.* 2014; January 2014, article 9. doi: 10.1155/2014/787968.

Montréal. CHEST 2015. Everyone's a winner

We all know that with the great success of CHEST 2015, everyone who shared that event is a winner. But, we would especially like to call out some of the special winners who were recognized during the meeting. Congratulations to all!

CHEST Awards

College Medalist Award
David D. Gutterman, MD, FCCP
Distinguished Service Award
John E. Studdard, MD, FCCP
Master Fellow Award
Kalpalatha K Guntupalli, MD, FCCP
Alton Ochsner Award Relating Smoking and Health
Sir Richard Peto, FRS
Alfred Soffer Award for Editorial Excellence
Peter J. Barnes, DM, Master FCCP
Paul M. O'Byrne, MBBCh, FCCP
Distinguished Service Award
John E. Studdard, MD, FCCP

Eli Lilly and Company Distinguished Scholar in Critical Care Medicine

Ognjen Gajic, MD, FCCP
CERTAIN Rounds: International Collaboration to Improve Critical Care Practice
Supported by Eli Lilly and Company

Foundation Grant Winners

2015 Research Grantees

Chiara Rigobello, PhD
University of Padua, Italy
The CHEST Foundation and the Alpha-1 Foundation Research Grant in Alpha-1 Antitrypsin Deficiency
Investigation of Susceptibility Factors in Alpha-1 Antitrypsin Deficiency: A Whole Exome Approach
Jointly supported by the CHEST Foundation and the Alpha-1 Foundation

Katrina Steiling, MD, MSc
Boston University School of Medicine
The CHEST Foundation Research Grant in Chronic Obstructive Pulmonary Disease
Characterizing Molecular Subphenotypes of Chronic Obstructive Pulmonary Disease
Supported in part by AstraZeneca

Debasree Banerjee, MD, MS
Rhode Island Hospital
The CHEST Foundation Research Grant in Pulmonary Arterial Hypertension
Sudden Cardiac Death in Pulmonary Arterial Hypertension: The Role of the Sodium Channel
Supported in part by Actelion Pharmaceuticals, US, Inc.

Martina Sterclova, MD, PhD
Thomayer Hospital, Czech Republic
The CHEST Foundation Research Grant in Pulmonary Fibrosis
New Methods of Diagnosis and Treatment in Individualization Considering Outcome Indicators in Patients With Interstitial Lung Disease
Supported in part by Genentech

Tetyana Kendzerska, MD
Sunnybrook Research Institute, Canada
The CHEST Foundation Research Grant in Women's Lung Health
A Risk Stratification Model for Adult Patients With Obstructive Sleep Apnea: Development and Evaluation—Cardiovascular Consequences of Obstructive Sleep Apnea in Women
Supported in part by AstraZeneca

Dale Hardy, PhD
Georgia Regents University
The CHEST Diversity Committee Minority Investigator Research Grant
Racial Disparities in Early Palliative Care Within Sociogeographic Regions for Elderly Patients With Lung Cancer
Jointly supported by CHEST and AstraZeneca

2015 Community Service Grantees
Supported in full by the CHEST Foundation.

Mary Hart, MS, RRT
University of Texas Health Science Center
CHEST Foundation Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP
Asthma Boot Camp

Vanessa Kerry, MD, MSc
Seed Global Health
CHEST Foundation Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP
Strengthening Critical Care Training and Care at Muhimbili University of Health and Allied Sciences, Tanzania

William Thompson, MD, FCCP
Seed Global Health
CHEST Foundation Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP
Expanding Bronchoscopy Training at Muhimbili Hospital for Tanzania

Zehra Surani, MS, RRT
It's Your Life Foundation
CHEST Foundation Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP
iConquer: Clean Wisely!

Honor and Memorial Lectures

Darcy D. Marciniuk, MD, FCCP
Thomas L. Petty, MD, Master FCCP Memorial Lecture
This award honors Thomas L. Petty, MD, Master FCCP, who trained hundreds of physicians in COPD, oxygen therapy, and spirometry. This award is conferred to a CHEST Fellow (FCCP) known for his or her work in advancing the understanding of COPD pathogenesis and/or treatment and for exceptional mentoring and clinical instruction skills.

Alessandro Brunelli, MD
Distinguished Scientist Honor Lecture in Cardiopulmonary Physiology
This lecture, established in 1973, is awarded to a well-respected and published original investigator in pulmonary clinical physiology.

Arthur P. Wheeler, MD, FCCP
Presidential Honor Lecture
This award chosen by the current CHEST President, honors an outstanding faculty member. One recipient is chosen each year based on his or her expertise in chest medicine.

John R. Bach, MD, FCCP
Margaret Pfrommer Memorial Lecture in Long-term Mechanical Ventilation
This award, established in 1999 by Dr. Eveline Faure and Dr. Allen I. Goldberg, honors their lifelong colleague and friend, Margaret Pfrommer, a polio survivor and patient advocate. It is awarded to a clinician or ventilator-dependent professional or advocate who has advanced mechanical ventilation and fostered partnerships between physicians and patients.

Praveen N. Mathur, MBBS, FCCP
Pasquale Ciaglia Memorial Lecture in Interventional Medicine
This award honors a CHEST member well known for his or her work in interventional medicine, such as clinical state-of-the-art innovations, economic impact, invention, interventional critical care, research opportunities, and/or a host of other interesting facets of interventional medicine.

Charles L. Sprung, MD, FCCP
Roger C. Bone Memorial Lecture in Critical Care
Established in 1997 to honor Roger C. Bone, MD, Master FCCP, a leader in critical care, sepsis, and sepsis research. Dr. Bone empowered physicians to communicate with patients and families about end-of-life issues and had significant achievements with CHEST.

Paul H. Mayo, MD, FCCP
Edward C. Rosenow III, MD, Master FCCP/Master Teacher Honor Lecture
This endowment, established in 2004, recognizes Dr. Edward C. Rosenow, who has promoted the development and training of hundreds of chest physicians during his 3 decades at the Mayo Clinic. It acknowledges his role of mentoring pulmonary and critical care physicians into CHEST leadership roles, where he has fostered the development of physicians-in-training to improve patient care.

Kenneth N. Olivier, MD, MPH, FCCP
Murray Kornfeld Memorial Founders Lecture
This lecture was established in 1974 in memory of Murray Kornfeld, founder of the Federation of American Sanatoria, which later became CHEST. This award is conferred to a leader in pulmonary and critical care medicine, particularly in infection and inflammation, who is developing therapies expected to guide medicine into the future.

CHEST Challenge Championship 2015
1st Place
Cleveland Clinic
Anupam Kumar, MBBS
Louis Lam, MD
Sameep Sehgal, MBBS
PD: Rendell W Ashton, MD, FCCP
2nd Place
University of Texas Health Science Center at Houston
Karunakar Akasapu, MD, MBBS
Sujith V Cherian, MD, MBBS
Lilit Sargsyan, MD
PD: Bela Patel, MD, FCCP
3rd Place
Maimonides Medical Center
Pavan Kumar Gorukanti, MD
Pavan K Irukulla, MD, MBBS
Mangalore Amith Shenoy, MBBS
PD: Yizhak Y Kupfer, MD, FCCP

Case Report Winners
Christine Bielick, MD (tied with Dr. Ahuja)
Shilpi Ahuja, MD (tied with Dr. Bielick)
Brian Walsh, DO
Naseem Alavian, MD
Rahul Sangani, MBBS

Continued on following page

Changing the publishing paradigm of *CHEST*

BY STEPHEN J. WELCH
SENIOR VICE PRESIDENT AND PUBLISHER, PUBLICATIONS AND DIGITAL CONTENT

Note: This article excerpts content from the January 2016 CHEST *editorial (Irwin RS, Welch SJ, Rice J, French CT. Spread the word about* CHEST *in 2016: An ever-rising impact factor, content innovations, launching a new partnership with Elsevier, and protecting the name and legacy of the journal.* Chest. *2016;149(1):1-6).*

Since its inception in 1935, *CHEST* had been self-published by the American College of Chest Physicians. Starting this month, January 2016, CHEST has chosen to work in partnership with Elsevier as its publisher. While CHEST will maintain editorial control over the journal, this partnership will allow us to grow the reach and awareness of the journal, provide world class data reporting and trend analysis, increase our outreach for the best clinical research in the field, and provide a competitive business backbone to increase our support for the CHEST organization. We are confident that the global footprint of Elsevier, its Science Direct and Clinical Key content delivery platforms, and its commitment to attracting the best clinical science for the journal, will provide the resources for *CHEST*

Continued on following page

Continued from previous page

Bravein Amalakuhan, MD
Lindsay Somerville, MD
Sunjay Devarajan, MD
Jey Chung, MD
Jennifer Butler, MD
Nicholas Fiacco, MD
Sheila Habib, MD
Anita Oh, MD
Jason Filopei, MD
Annalee de Leon-Manalo, MD
Pooja Desa, MD, MBBS
Abhinav Gupta, MD, MBBS
Daniel Burke, MD
Adam Fox, MD
Alexandra Perry, MD

Alfred Soffer Award Winners
Allain Tremblay, MD, FCCP
Ehab Billatos, MD

Top 3 Posters
Nadine Strilchuk, NP, MN
April Plank, NP, MSN
Steven Keller, MD, PhD

Young Investigator Award Winners
Sebastian Ochoa, MD
Allison Lambert, MD

CHEST Bingo Winners
Sarah Thyen
Authur Crisostomo, MD, FCCP
Michelle Miller, MD
Rakesh Bhargava
Cem Gundogdu
John Belany, DO, FCCP
Randeep Guleria Sr., MD
Mary Carmen Rodriguez
Firas Koura, MD, FCCP
Asma Iftikhar, MD
Kyle Le, PA-C
Jeana Handley
Christie Rocke, MSN, APN
James Spence, MD, FCCP
William Hutchens, MD, FCCP

Continued from previous page

to continue to evolve, innovate, and bring our readers the most relevant, cutting-edge content to help them provide the best patient care every minute of every day. Please join us in celebrating a new relationship that we believe will benefit our readers, our parent CHEST organization and its membership, and our new business partner, Elsevier.

Elsevier content innovations and benefits for authors and readers

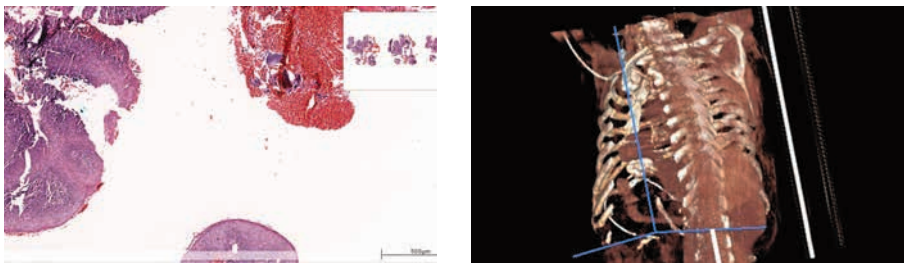
Some exciting new content innovations will be available to *CHEST* authors and readers through Elsevier's Science Direct platform.

These will include (1) a virtual microscope that will allow authors to submit high-resolution figures that can be viewed and zoomed in to great detail not previously possible (Figure, left); (2) interactive case reports that will allow us to modify case-based sections like Pearls and Chest Imaging so that the reader has to select the right answer from multiple choices; (3) multimedia audio slide summaries that will allow authors to record up to a 5-minute audio file, with slides, that summarizes their paper; and (4) interactive 3-D radiologic imaging that will allow conversion of images to an interactive 3-D model (Figure,right). These innovations will be implemented throughout 2016, and instructions on how to use them have been added to our Instructions to Authors, which can be found at: http://journal.publications.chestnet.org/ss/forauthors.aspx

We are actively assessing other innovations that may be implemented at a later date. A list and description of the content innovations discussed above, as well as ones we are considering, can be found at:

https://www.elsevier.com/books-and-journals/content-innovation#list.

In addition, the partnership with Elsevier will allow for a number of benefits to authors and readers. First of all, we will no longer charge authors for submission of color figures. We believe this will enhance the visual appeal of articles and provide more clarity when looking at data plots and graphs, as color will be easier to discern than gray scale. In addition, Elsevier teams will redraw figures and use color in graphs and charts where appropriate to create consistency in the look and feel of the journal, improving readability and data interpretation by the reader. Second, Elsevier will provide an author dashboard, so that the author can see information about their article, such as citation statistics and bibliometrics, as well as usage and downloads. And, in order to facilitate wider dissemination of our correspondence, we are moving that section from an online-only status and putting it back into the print journal, as well as online. We are excited to offer all of these services to our authors and readers.



Left, Example of viewing a figure with the virtual microscope. Right, Example of new interactive 3-D radiologic imaging for figures.

We want to assure our authors that all of these content innovations and benefits will be free of charge!

Innovation is not new for *CHEST*. A blog on *The Scholarly Kitchen*, written by Kent Anderson, noted "One frequent design challenge for both print and online is to make multimedia content more apparent to online users. The *CHEST* redesign is notable in this regard, as the editorial explaining it carefully demonstrates how to access video, audio, and data options around articles. It reads like an instruction manual, which is not a criticism. Change has to be handled carefully, and most journals (and organizations in general) under-communicate changes and benefits to their customers. On the strategic front, the *CHEST* redesign is geared to providing more online-only content, a strong trend among journals, especially as print advertising continues a slow and steady decline." http://scholarlykitchen.sspnet.org/2014/07/07/the-journal-redesign-more-complicated-more-costly-and-more-strategic-than-ever/

We would be remiss if we didn't thank you, our readers, members, authors, contributors, and peer reviewers, for the important roles you play in ensuring the success of our efforts to provide the best clinical content to the *CHEST* readership. Thank you for your ongoing support and contributions to *CHEST*.

This month in *CHEST*: Editor's picks

BY DR. RICHARD S. IRWIN, MASTER FCCP
EDITOR IN CHIEF, *CHEST*

Spread the Word About CHEST in 2016: An Ever-Rising Impact Factor, Content Innovations, Launching a New Partnership With Elsevier, and Protecting the Name and Legacy of the Journal. *By Dr. R. S. Irwin et al.*

Defining the Asthma-COPD Overlap Syndrome in a COPD Cohort. *By Dr. B. G. Cosio et al.*

Practice Patterns and Outcomes of Treatments for Atrial Fibrillation During Sepsis: A Propensity-Matched Cohort Study. *By Dr. A. J. Walkey et al.*

Postoperative Complications in Patients With Unrecognized Obesity Hypoventilation Syndrome Undergoing Elective Noncardiac Surgery. *By Dr. R. Kaw et al.*

Treatment of Unexplained Chronic Cough: CHEST Guideline and Expert Panel Report. *By Dr. P. Gibson et al.*

Evaluation of Occupational and Environmental Factors in the Assessment of Chronic Cough in Adults: A Systematic Review. *By Dr. S. M. Tarlo et al.*

Live like a local!

When you travel to Shanghai, China for CHEST World Congress 2016, you will be immersed in a wonderful Chinese culture complete with flavorful, authentic food; exquisite, local architecture and gardens; and a native language with beautifully written characters. While we encourage you to take in all the famous tourist spots, we also challenge you to live like a local and come prepared and knowledgeable so that you'll get the most from your Shanghai experience.

Don't leave home until you've read our tips for enjoying your stay in Shanghai:

1. **Water.** Don't drink tap water in Shanghai. Bottled water is widely available. It is OK to brush your teeth with tap water at hotels.
2. **Money.** Your international credit card will only be accepted at top hotels, restaurants, and shops that cater to foreigners, and many credit cards have hidden fees when travelling internationally. Make sure to leave home with some money exchanged to RMB yuan (¥). If you need more money while you're in Shanghai, the airport, hotel banks, and larger branches of the Bank of China can exchange money for you. Or, before you leave home, check with your bank to find out which local ATMs will exchange currency from your credit card.
3. **Tips.** There is officially no tipping in China, but it has become commonplace for bellhops, tour guides, and tour bus drivers to receive tips. You do not need to tip taxi drivers or restaurant employees.
4. **Electricity.** The electricity in China is generally 220V. Most North American electrical devices will require a transformer. Outlets come in a variety of configurations, so it may be hard to plan ahead, but you can purchase transformers or adapters at department stores.
5. **Bathrooms.** Don't rely on public restrooms because many will not meet your expectations, and they don't always provide tissues or soap. However, you can usually find a restroom more similar to what you are used to at big hotels, restaurants catering to foreigners, and newer malls.
6. **Language.** English is seldom spoken by locals. However, younger locals should recognize at least some English from their mandatory English classes in school. Mandarin is the official language in China, but locals may also converse in Shanghainese.

Continued on following page

Continued from previous page

7. **Shopping.** You should expect to bargain for the best price at street and small private stores. Try to compromise on price and smile through your negotiations. Beware of knock-offs, especially at markets. Jade is particularly prone to be fake.
8. **Avoiding offense.** It is very important not to cause someone to lose face in public. This is considered to be highly offensive. Avoid losing your temper or calling someone out in public. Take up matters privately, when needed.
9. **Smoking.** Smoking is very popular in China, and it is not restricted nearly as much as it is in North America. There is a smoking ban on public transit, and nonsmoking rooms are available upon request at hotels. Some restaurants have nonsmoking sections.
10. **Climate and time zone.** Spring is a great time to travel to Shanghai. April's temperatures are generally in the 60s with some light rain. Shanghai is 13 hours ahead of New York, 14 hours ahead of Chicago, and 16 hours ahead of Los Angeles. You may feel jetlagged and need time to adjust to the drastic change.
11. **Emergency.** Here are the local emergency numbers: Fire: 119, police: 110, and ambulance: 120.
12. **Transportation.** The best way to get around town is either by taxi or on the metro. Learn more about the Shanghai Metro at http://service.shmetro.com/en.

With all these tips in mind, we hope you'll be prepared to thoroughly enjoy your stay in Shanghai. During CHEST World Congress 2016, April 15 - 17, you'll feel right at home with presentations in English and top-notch education and simulation sessions that you've grown to expect from CHEST. Learn more about CHEST World Congress at chestnet.org/CWC2016.

CHEST Foundation update

During this past year, the CHEST Foundation reached impressive new heights. Nearly a half a million dollars in research grants was awarded, with over $41,000 supporting community service programs ranging from critical care training in Tanzania to asthma education camps for the underserved children in San Antonio, Texas.

Our Disease Awareness Campaigns remain stronger than ever, reaching millions of sports fans at the Daytona 500, Brickyard 400, NASCAR Sprint Cup Race at Chicagoland, and the Indianapolis 500 with lung health public service announcements. In addition to the wide-reaching campaigns, our partnership with the American Lung Association will result in patient education information on 40 lung disease topics, some of which are already accessible on the ALA website, lung.org.

More than 95 cents of every dollar raised by the CHEST Foundation goes toward advancing our mission-based programming.

The CHEST Foundation is making a substantial impact on worldwide lung health. More than 95 cents of every dollar raised by the CHEST Foundation goes toward advancing our mission-based programming. Every cent and every donation matters: $100 can support the cost to print 250 "Healthy Lungs Passports" for children; $250 can supply a pulmonary reference textbook for physicians in Tanzania; $500 would help cover travel expenses for 20 home visits to teach children with asthma, and their parents, how to better control their condition; and $750 could fund a laptop computer and projector used to deliver chest medicine training for medical personnel in Africa.

With each contribution, our ability to make an impact on global lung health strengthens. We would like to thank all of our donors for being advocates for our mission—to champion lung health. Our list of achievements and successes is long because of the important role that our members play in ensuring the CHEST Foundation's efforts to build healthier communities and save lives.

We hope that you will continue to embrace the foundation with enthusiasm, and include us in your end-of-year giving. To make a donation and learn more about the foundation, visit chestnet.org/foundation, or call us at 224/521-9527.

CHEST® FOUNDATION

In memoriam

Dr. Arthur P. Wheeler, FCCP, died on December 17, 2015. He attended undergraduate school (UMBC) and medical school (UMAB) at The University of Maryland. He moved to Nashville, Tennessee, in 1982 for residency training at Vanderbilt University Medical Center and remained there for his entire professional career. He was Director of the Medical Intensive Care Unit at Vanderbilt University Hospital for 22 years, where he had a prolific research career that primarily focused on the development of new treatments for ARDS through the ARDSnet Team, leading to improved survival for many patients. His passion for teaching and for understanding how best to care for critically ill patients will be missed by his many colleagues and friends who he inspired throughout the years. Art's involvement with the American College of Chest Physicians spanned almost 30 years and included serving on the editorial boards of *CHEST* and *CHEST SEEK Critical Care*. He recently was honored in *CHEST* as a Giant in Chest Medicine. Art often shared that he considered participating in SEEK as one of his most favorite and rewarding professional activities. *CHEST SEEK Critical Care: 26th Edition* will be dedicated to Dr. Wheeler. We extend our heartfelt condolences to his wife, Lisa, and the entire Wheeler family.

Physician Compare: Expanded data cause concern

BY ALICIA GALLEGOS
Frontline Medical News

Potentially inaccurate data posted on the federal Physician Compare website could misinform patients and lead to incorrect assumptions about the quality of care individual doctors provide.

With the most recent update of Physician Compare, the Centers for Medicare & Medicaid Services for the first time has posted individual physician performance scores on the 40,000 individual health care professionals who are part of the Physician Quality Reporting System (PQRS).

"Given the widespread accuracy issues with the 2014 PQRS calculations, the newly released information is premature," American Medical Association President Steven J. Stack said in a statement. "The data inaccuracies and difficulties with CMS's processes grew over the last couple of months and, while CMS has acknowledged these problems, it has failed to address the underlying issues. Most importantly, consumers visiting the Physician Compare website are likely to get a false impression that it provides accurate quality information for all physicians, when in fact, due to significant data problems, the newly added information covers only about 40,000 physicians."

Although the concept of Physician Compare makes sense, the CMS needs to resolve data inconsistencies and improve how the information is being presented before posting new information to the site, said Dr. Wanda Filer, president of the American Academy of Family Physicians (AAFP). Performance scores on each measure are displayed on Physician Compare as stars followed by a percent, with each star representing 20%.

"A star rating system is too simplistic to provide for informed decisions [and] doesn't reflect the complexity or context of care that undergirds those measures," Dr. Filer said in an interview. "Given that complexity, it is likely that inaccurate data will be attributed to a physician's care."

In an effort to reduce inaccuracies, the AAFP had called for an extended period – from the current 30 days to 90 – for physicians to review their data before the data are published, Dr. Filer said.

The CMS takes too long to communicate with physicians about their performance scores. Doctors do not receive reports for 6-9 months, reducing the opportunity for them to improve their performance before the next reporting period, she said.

"Moreover, CMS must do a better job educating physicians about this website and their opportunity to review and correct any inaccuracies," she added.

In addition to posting new PQRS measures on Physician Compare, the CMS also has posted 2014 data from group practices that report patient experience measures through the Consumer Assessment of Healthcare Providers and Systems (CAHPS) for PQRS survey. The CAHPS survey measures Medicare patients' feedback about their care experiences. Updated performance scores for accountable care organizations, including clinical quality of care and patient experience measures for Shared Savings Program ACOs and 20 Pioneer ACOs were also added.

VIEW ON THE NEWS

Dr. Michael E. Nelson, FCCP, comments: In case you are unaware, there are multiple different websites where everything from your clinical skills to your waiting times are rated by whomever wants to log on and rate you. These sites are being utilized by the increasingly tech-savvy patient to modify your reputation, for better or worse. Enter your friends in the federal government who have been collecting data from the Physician Quality Reporting System (PQRS) and have now provided that for public review. Unfortunately, the PQRS data tells little about you as a person. Rather, it informs the uninformed how often you prescribed an inhaler to someone with an FEV_1/FVC ratio less than 60% or documented their spirometry results. Personally, I wish they would have spent their time and my money (tax dollars) on something of greater benefit to patients, leaving Angie, Healthgrades, Zocdoc, Consumer Reports, etc. to do the ratings.

agallegos@frontlinemedcom.com
On Twitter @legal_med

AMA to CMS: Delay meaningful use Stage 3

BY ALICIA GALLEGOS
Frontline Medical News

The American Medical Association is asking the Centers for Medicare & Medicaid Services to revise the meaningful use program to better align with requirements of last year's Medicare Access and CHIP Reauthorization Act (MACRA) and to allow for smoother transition to value-based payment models.

In a letter to CMS, the AMA issued a list of recommendations for meaningful use Stage 3 that aim to address challenges with using electronic health records (EHRs) and to help move toward MACRA's alternative payment models (APM) and Merit-Based Incentive Payment System (MIPS).

"Doctors want to spend their time with patients, not measuring the number of clicks," Dr. Steven J. Stack, AMA president, said in a statement. "We want a successful transition to digital health records, and we also want the new Medicare law to succeed. It will take thoughtful changes in the regulations to support physicians as they treat patients through new models of care."

The AMA's recommendations come in response to CMS' final rule for meaningful use Stage 3, effective Dec. 15. The final rule simplified Stage 3 and gave doctors 1 more year – until Jan. 1, 2018 – to comply.

The AMA requested that CMS immediately adopt the association's revisions for meaningful use Stage 3, including that the agency provide more flexibility and allow for multiple methods/paths to achieve desired end goals; remove threshold requirements for measures outside physicians' control; and eliminate its pass-fail program design. Scrapping a pass-fail approach is the only way the ... program can align and operate within MIPS and APMs, Dr. James L. Madara, AMA executive vice president and CEO wrote in the letter.

The AMA also criticized Stage 3 for taking a poor approach to interoperability. The current measures are too focused on the quantity of information moved and "not the relevance of exchanges or the underlying business case for transmitting data," Dr. Madara wrote. The AMA wants the measures to be refocused to address specific instances of data exchange, such as closing the referral loop, team-based care, and notification of tests/admissions.

According to the AMA, CMS should:

- Re-orient measures away from process-based tasks to highlight goals that are useful to patients and physicians.
- Encourage new technology functions to be the focus of certification rather than placing requirements on physicians and patients that may not yet be feasible.
- Support the reuse of data to reduce the burden on documentation.

The AMA's recommendations are in line with concerns by the American Academy of Family Physicians over Stage 3, according to Dr. Robert L. Wergin, AAFP board chair. In a Dec. 2 letter to CMS, the AAFP said the final rule fell short of expectations and, in fact, places further obstacles in the way of improved health, better health care, and lower cost.

"I would call it a potential unrealized. It really hasn't developed into what we thought it could do. There's a lot of frustrations," Dr. Wergin said.

The AAFP calls for CMS to hit the pause button on meaningful use until 2019 – long enough to allow:

Continued on page 34

VIEW ON THE NEWS

Dr. Michael E. Nelson, FCCP, comments: Despite protestations from physicians, societies, and Congress, CMS plans to move forward with Meaningful Use regulations. Those who have attempted to achieve "meaningful use" recognize that this achievement does not necessarily translate into better patient care. Indeed, hunting and pecking on one's computer to capture necessary data probably lessens the time the busy physician can focus on the patient. As the article states, interoperability, an item that would positively affect patient care but not under the direct control of the physician, continues to be the major "information roadblock." Penalizing physicians because their computers don't communicate will certainly increase dissatisfaction and likely lessen compliance. On December 31st, CMS released a *Request for Information: Certification Frequency and Requirements for the Reporting of Quality Measures under CMS Programs*. I would encourage everyone to send their thoughts to CMS.

CLASSIFIEDS

Also available at MedJobNetwork.com

PROFESSIONAL OPPORTUNITIES

Central Maine Medical Center
The Central Maine Medical Family

Inpatient Pulmonary/Critical Care Position in Maine:

Join a vibrant Inpatient Pulmonary and Critical Care group of five in beautiful Maine! Central Maine Medical Center (CMMC) is seeking a BC/BE Pulmonary/Critical Care Physician to help provide pulmonary and critical care services to medical, surgical, trauma, and cardiac patients.

CMMC is a 250 bed, full service regional referral center with busy trauma, cardiothoracic, interventional radiology, vascular, and neurosurgical programs. We have a state-of-the art 19 bed ICU and a separate 16 bed cardiothoracic unit.

Competitive salary and benefits including CME, paid vacation, student loan repayment, 403b match, and relocation fees. Work schedule revolves around a 6 day on and 6 day off philosophy, with no longer than 12 hour shifts per day. There is no outpatient clinic work.

Residents and visitors enjoy an extraordinary lifestyle that revolves around top school systems, ski resorts, lake and ocean water sports, theatre, and world-class dining.

Interested applicants may submit CV to Julia Lauver, Medical Staff Recruiter, Central Maine Medical Center, 300 Main Street, Lewiston, ME 04240. Email: JLauver@cmhc.org . Fax: 207/795-5696. Call: 800/445-7431. Visit our website, www.cmmc.org.

Pulmonology/ Intensivist

Join eight university trained, Board Certified Pulmonary, Critical Care and Sleep Medicine physicians. Our integrated multi-specialty physician clinic and hospital includes a Level II Trauma Center and an accredited sleep center. Practice with strong colleagues in the region's tertiary referral center.

#1 Hospital in Montana
U.S.News & WORLD REPORT

Contact: Rochelle Woods
1-888-554-5922
physicianrecruiter@billingsclinic.org

Physician-Led Medicine in Montana

Billings Clinic is nationally recognized for clinical excellence and is a proud member of the **Mayo Clinic Care Network.** Located in the magnificent Rocky Mountains in Billings, Montana, this friendly college community has great schools, safe neighborhoods and family activities. Exciting outdoor recreation minutes from home. 300 days of sunshine!

Billings Clinic

billingsclinic.com

PRESBYTERIAN

PULMONARY / CRITICAL CARE PHYSICIAN

Presbyterian Healthcare Services (PHS) is seeking a Pulmonary/Critical Care trained physician to join our established group.

The physician will consist of 75% Critical Care and 25% Pulmonary.

PHS is a non-profit integrated health-care system that employs over 600 providers and includes a healthplan.

Benefits include medical, dental, vision, 403(b) plus match, CME, malpractice coverage (tail insurance included), competitive salary, sign on bonus and relocation assistance.

For more information, please contact:
Kelly Herrera
505-923-5662
kherrera@phs.org

Memorial Healthcare System

Critical Care Medicine Employment Opportunity

Join a Leading Healthcare System in South Florida

Memorial Healthcare System is seeking an Intensivist, dedicated to night shifts, to join the critical care team. Successful candidates will demonstrate excellent clinical skills, a broad knowledge base and dedication to providing high quality, evidence-based patient care. Applicants must be BE/BC in critical care medicine. Currently, the critical care program includes 28 full-time intensivists and six critical care ARNPs. The successful candidate will integrate into the existing operational structure, joining the team of eight dedicated full-time nocturnists.

- 12-hour in-house shifts (7 pm – 7 am); no responsibilities outside of in-house shifts
- Approximately 12 – 14 shifts per month (more if desired)
- Highly competitive salary differential for the nocturnist position

This is a full-time employed position within the multispecialty Memorial Physician Group. The position offers competitive benefits and a compensation package that is commensurate with training and experience. Professional malpractice and medical liability are covered under sovereign immunity.

About Memorial Healthcare System

Memorial Healthcare System is the third-largest public healthcare system in the United States. A national leader in quality care and patient satisfaction, Memorial has ranked 11 times since 2008 on nationally recognized lists of great places to work – in Modern Healthcare magazine, Florida Trend magazine and Becker's Hospital Review, just to name a few.

Memorial's facilities include its flagship, Memorial Regional Hospital, one of the largest in Florida; Memorial Regional Hospital South; Joe DiMaggio Children's Hospital, the only freestanding children's hospital in Broward and Palm Beach counties; Memorial Hospital West; Memorial Hospital Miramar; Memorial Hospital Pembroke; and Memorial Manor, a US News five-star-rated nursing home.

Memorial's work environment has been rated by employees and physicians alike as an open-door, inclusive culture that is committed to safety, transparency and above all, outstanding service to patients and families.

memorialphysician.com

mhsemp072

WANTED

Pulmonary/Critical Care Physician. Pulmonary Consultants P.C. located in Phoenix Arizona is a Six-Doctor Pulmonary/Critical group seeking additional Physician due to practice growth. Diverse Hospital/office practice encompassing pulmonary, critical care medicine. Competitive salary/excellent benefits. Please send your CV via fax to 480 218-5706 or email to **aliciaga@PCofMesa.com** cell 480-466-2612

It's a Brand New Day for CHEST Logo Products

> **Purchase at:** chestcollection.com

CHEST
AMERICAN COLLEGE of CHEST PHYSICIANS

KEEP UP-TO-DATE
Watch our Classified Notices for Postgraduate Course Information.

Moving? Look to Classified Notices for practices available in your area.

Disclaimer

Chest Physician assumes the statements made in classified advertisements are accurate, but cannot investigate the statements and assumes no responsibility or liability concerning their content. The Publisher reserves the right to decline, withdraw, or edit advertisements. Every effort will be made to avoid mistakes, but responsibility cannot be accepted for clerical or printer errors.

CLASSIFIEDS

Also available at MedJobNetwork.com

PROFESSIONAL OPPORTUNITIES

Mid-South Pulmonary Specialists P.C.

Large private practice group looking for a Critical Care Intensivist needed for 40 bed CVICU in Memphis, Tennessee.

6pm-7am. 7 Days on /7 days off. Highly competitive salary plus benefits including 401(k)/ pension/health insurance. Large multi-cultural city located along the beautiful Mississippi River with lots of outdoor activities. Interested parties please send CV to **kwavery@mspulmonary.com**

WISCONSIN

MINISTRY HEALTH CARE

PULMONOLOGY /CRITICAL CARE OPPORTUNITY UPPER MIDWEST

Ministry Health Care is actively seeking a BC/BE Pulmonology/ Critical Care physician for a growing program at our 110-bed tertiary referral center in Weston, WI. This is an excellent opportunity to join a financially sound, physician-led organization, treat a broad scope of cases and play a significant role in the growth and success of our program.

- Call is 1:4
- 12+ ICU bed coverage with significant support from Hospitalist team, Anesthesia and E-ICU
- EBUS and EUS on site; would support any procedures you were interested in
- Strong, established referral network
- Digitally advanced facility consistently named one of the nation's "Most Wired" hospitals

You'll enjoy an excellent quality oflife in the Wausau/Weston area. The community is vibrant, safe and affordable and offers a full complement of metropolitan amenities complete with a downhill ski resort and a regional airport.

CONTACT: BRENDA CHAMBERS (715) 342-6579
mmgrecruitment@ministryhealth.org
www.ministryhealth.org

OHIO
CRITICAL CARE MEDICINE - DAYTON, OH

Excellent opportunity for BC/BE CCM physician to join growing 36+ physicians' private practice CCM/ID/Hospitalist/Endocrine group. Dayton is located in southwestern, OH. The metropolitan area of 800,000 offers many cultural, sports and recreational activities, excellent public and private school systems and affordable housing. Competitive salary and outstanding benefit package. Not a J-1 Visa opportunity.

Send CV or call:

Becky Kronauge
Practice Administrator
33 West Rahn Rd
Dayton, OH 45429
PH:(937)433-8990 ext.124
FAX:(937) 433-8691
Email: **rkronauge@sdacc.com**
Web: **www.sdacc.com**

CHEST Physician
CLASSIFIEDS

For Deadlines and More Information, Contact:
Lauren Morgan
Tel: (267) 980-6087
lmorgan@americanmedicalcomm.com

FRONTLINE MEDICAL COMMUNICATIONS

Disclaimer

Chest Physician assumes the statements made in classified advertisements are accurate, but cannot investigate the statements and assumes no responsibility or liability concerning their content. The Publisher reserves the right to decline, withdraw, or edit advertisements. Every effort will be made to avoid mistakes, but responsibility cannot be accepted for clerical or printer errors.

Continued from page 31

• The health care industry time to focus on interoperability issues.
• Vendors, physicians, and other health care professionals time to focus on designing and implementing the functionality and work flows necessary to achieve value-based payment.
• Regulators time to modify meaningful use regulations and align them with pending MACRA rules.

Similar concerns were expressed in a letter from the GOP Doctors Caucus to Speaker of the House Paul Ryan (R-Wisc.). The 18-member caucus requested Speaker Ryan's help in pressing for a delay of Stage 3 and a blanket hardship waiver exception for Stage 2. Implementation of more-stringent criteria is likely to create "a chilling effect on further EMR adoption as physicians conclude that the cost of implementation is simply not worth the bureaucratic hassle," according to the letter. "Members of our caucus, as well as numerous congressional health care leaders, have engaged CMS on these issues to warn them of the potential negative consequences of placing these new requirements on providers in order to meet an arbitrary deadline. CMS has ignored Congress. Congressional action is the only solution left for preserving patient access, choice and quality."

But Dr. Rocky D. Bilhartz, an interventional cardiologist in College Station, Tex., does not believe that the AMA's recommendations nor other changes to the meaningful use program will make it better. "I think they're going about this entirely the wrong way," said Dr. Bilhartz who blogs at bilhartzmd.com. "Meaningful use should not be delayed, but frankly abandoned. I don't necessarily believe that the Department of Health & Human Service set out to try to design a system that would impair a physician's ability to care for patients. I do believe without a doubt, that is exactly what has happened."

agallegos@
frontlinemedcom.com
On Twitter @legal_med

Failing to account for DNRs could result in penalties

BY AMY KARON
Frontline Medical News

Mortality-based quality measures that do not account for do-not-resuscitate orders paint a skewed picture of hospital performance, said authors of a multicenter retrospective cohort study.

"Current methods of comparing hospitals, which do not account for patient DNR status, penalize potentially high-quality hospitals [that admit] a larger proportion of patients who had chosen to forgo resuscitation," Dr. Allan J. Walkey of Boston University, and his associates wrote in JAMA Internal Medicine.

The study assessed DNR status and mortality for more than 90,000 pneumonia cases at 303 hospitals in California during 2011 (JAMA Intern Med. 2015 Dec. 14. doi: 10.1001/jamainternmed.2015.6324).

The lower and upper quartiles for DNR rates were about 9% and 22%. Without accounting for these differences, hospitals in the highest quartile had significantly greater patient mortality (adjusted odds ratio, 1.17; 95% confidence interval, 1.04-1.32). But this trend actually reversed after accounting for DNR rates (adjusted OR, 0.79; 95% CI, 0.70-0.89), as did the link between hospital mortality rankings and DNR rates. The study was funded by the NIH, the NHLBI, the Agency for Healthcare Research and Quality, the Edith Nourse Rogers Memorial VA Hospital, and Boston University.

VIEW ON THE NEWS

Dr. James A.L. Mathers Jr., FCCP, comments: This report, based on a study published in JAMA, accurately summarizes the findings; however, we are reminded that attempting to reduce the complex issue of quality of care to a few data points is a challenging endeavor. There are many variables in play when establishing a patient's and family's wishes in regard to resuscitation status, and the subsequent impact on care is unpredictable. This is just one of several reasons that many thought leaders favor the 30-day mortality measure over the in-hospital mortality measure.

NETWORKS: Allied Health, Cardiovascular Medicine and Surgery, Chest Infections, Clinical Pulmonary Medicine

Allied Health

Air travel and comorbidities

It is estimated that at least 5% of US airline passengers have preexisting medical diseases. Coupled with a rising number of aging passengers and longer flights, there is a growing need for preflight assessment and guidance for individuals with comorbidities, including those with pulmonary disease.

An article in the *New England Journal of Medicine* (2015;373[10]:939) examined in-flight medical emergencies during commercial travel. With an incidence of medical emergencies in 1 of 604 flights, syncope/presyncope (37.4%) and dyspnea (12%) were the most frequent symptoms encountered by air travelers. Cruising altitudes can reach 60,000 feet but routinely remain at 30,000-40,000 feet, while the cabin altitude pressure is usually 5,000 to 8,000 feet – the equivalent of air that contains 25% less oxygen at sea level (*Ann Am Thorac Soc.* 2014;11[10]:1614). For the healthy individual, this change may be of little consequence, but passengers with preexisting pulmonary disease may be at risk for significant hypoxemia. Use of FEV_1 and SpO_2 are not useful indicators of degree of hypoxemia at altitude or potential for in-flight or postflight respiratory emergencies (*Thorax.* 2014;66:i1). A discussion of the impact of altitude on the multitude of pulmonary disorders, such as COPD, pulmonary hypertension, restrictive lung disease, hypoxemia respiratory failure, obstructive sleep apnea, and interstitial lung disease, is beyond the scope of this article but highlights the need for ongoing research into screening of patients with comorbidities prior to flight.


MR. UNKLE

David Unkle, APRN
Steering Committee Member

Chest Infections

Diagnostics and stewardship

Respiratory tract infections account for the large majority of antibiotic prescriptions. However, despite antibiotic stewardship efforts, there is still a great deal of inappropriate use. Use of diagnostics has been proposed as a means to decrease this aberrant prescribing; however, to date, none has really had the sensitivity or specificity needed to base clinical decisions. For over a decade, there has been growing enthusiasm in Europe for the serum procalcitonin (PCT) test. Indeed, a Cochrane review (Schuetz et al. *Cochrane Review.* 2013;8:1297) concluded that PCT-guided therapy was not associated with increased clinical failures or mortality. To date, there have been few US based studies of the impact of PCT on respiratory tract infection management. A group from the University of Rochester have reported a second study of PCT in patients who were hospitalized with nonpneumonic LRTI (Branche et al. *Clin Inf Dis.* 2015;212:1692). This study was designed to assist physicians by using levels of PCT as a need for antibiotics. Patients were randomized to receive standard of care or treatment based on a multiplex of PCR studies and PCT levels. The authors report a shortening of antibiotic therapy by 2 days (P=.002) in those with a proven viral infection. It was concluded that the combination of rapid broad molecular assays in combination with serum PCT levels can reduce unnecessary antibiotic use. When one just considers that over 85% of all COPD patients will receive at least one course of antibiotics in their lifetime and yet only about 25% to 30% of infections are likely to be bacterial, these data may be useful for managing LRTI cases but, to date, there have been few large scale studies of PCT in hospitalized community-acquired pneumonia.


DR. TILLOTSON

However given these data, we should not be totally 'gung-ho' about adopting PCT in all clinics and offices. One must be aware of the role of comorbid conditions in driving elevated PCT levels, such as concurrent infections in, for example, the urinary tract, and there are procedures and serious events that can lead to increased PCT, eg, patients in cardiogenic shock.

Finally, it is important to realize that PCT tests are not universally available or paid for by all insurers. The test has to be performed by qualified technicians, the equipment and tests are quite costly, and, ironically, it can be "cheaper" to write a prescription for a generic antibiotic than to pay for a PCT test, no matter how quickly the results are available. The White House is rightly putting huge effort and support behind the National Plan to Combat Antibiotic Resistance, but we should not wait for a "simple" diagnostic test to turn the tide. Some more basic understanding of when and how to use antibiotics is urgently required.

Glenn S. Tillotson, PhD, FCCP
Past Chair

Cardiovascular Medicine and Surgery

Team approach to STEMI

Care of STEMI patients has been focused on early intervention with a goal of door to balloon time and symptom onset to balloon time of less than 90 and 240 minutes, respectively, with reduction in morbidity and mortality (De Luca et al. *JACC.* 2003;42:991). Success in meeting these time constraints in a public hospital with limited resources required a multidisciplinary approach focusing on four main core principles: recognition, treatment, accountability, and flexibility.


DR. TSAI

Recognition and treatment

Recognition begins the moment patients develop chest pain with education on appropriate ambulance transportation (Boothroyd et al. *Am J Cardiol.* 2014; 114[9]:1289; Tennyson JC and Quale MR. *Prehosp Disaster Med.* 2014;29[1]:50). Once a healthcare professional in the ED has made contact with the patient, recognition and confirmation of STEMI by ECG is done, the STEMI pager is activated. Treatment involves two trained cardiac cath lab personnel in-house (24/7) in 20 minutes or less. Once the interventional attending arrives, the case begins.

Accountability and flexibility

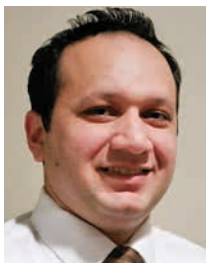
Accountability highlighted within the STEMI protocol can ensure personal responsibility along with individual and protocol-based assessment and improvement via constant, timely assessed feedback from STEMI leadership. Flexibility–the key factor–creates time cushions and multiple parallel response sequences keeping the STEMI protocol on schedule despite encountering certain "real life" obstacles. This gives the protocol its much needed "wiggle room" to keep each STEMI activation on track without losing sight of the overall goal, achieving the best times and outcomes and comparing favorably to others (Fosbol et al. *Circulation.* 2013;127[5]:604).

Dr. Peter I. Tsai, FCCP
Steering Committee Member
Dr. Nasser M. Lakkis

Clinical Pulmonary Medicine

Lung function reversibility

International guidelines define bronchodilator reversibility (BDR) as percent and absolute and change from the baseline in forced expiratory volume in first second (FEV_1) and/or forced vital capacity (FVC) ≥12% and 200 mL, respectively. However, a response below these threshold values may be associated with clinically relevant outcomes.


DR. ADRISH

In a retrospective analysis, BDR criteria were tested against the null hypotheses by Helen Ward, MBChB, of Queen Elizabeth Hospital, England, and her colleagues (*Chest.* 2015;148[4]:877).

They hypothesized that survival advantage must be seen in patients with "clinically important BDR."

Authors analyzed 16 year-long databases to determine expression of BDR; 4,227 patients aged > 20 years with $FEV_1 \geq 0.2$ L, $FEV_1/FVC \geq 0.2$, valid BDR testing and survival data were analyzed. Rank sum test was used for comparison, and Cox proportional hazards regression was used for survival analysis.

They noted that absolute change in FEV_1 led to significant bias in diagnosing reversibility in men and in subjects with higher absolute FEV_1 values. The method based on the change in the percent predicted, however, did not lead to a sex or a size bias and showed a survival cutoff of >8% predicted.

No benefit was observed by adding an absolute threshold of 200 mL and then 250 mL to percent predicted.

"We found that expressing BDR by the change in FEV_1 as percent predicted avoided any sex and size bias and gave the best survival prediction," they wrote. Authors did not report any funding.

Dr. Muhammad Adrish, FCCP
Steering Committee Member

EKOS®

History's greatest instruments really get the blood moving.

EKOS CORPORATION | 888.400.3567 | **EKOSCORP.COM**

BTG

FDA CLEARED INDICATIONS: The EkoSonic® Endovascular System is indicated for the ultrasound-facilitated, controlled, and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism; the controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature; and the infusion of solutions into the pulmonary arteries. Instructions for use, including warnings, precautions, potential complications, and contraindications can be found at www.ekoscorp.com. Caution: Federal (USA) law restricts these devices to sale by or on the order of a physician. **THE CE MARK (CE0086) HAS BEEN AFFIXED TO THE EKOSONIC® PRODUCT WITH THE FOLLOWING INDICATIONS:** ***Peripheral Vasculature:*** The EkoSonic® Endovascular Device, consisting of the Intelligent Drug Delivery Catheter (IDDC) and the MicroSonic™ Device (MSD), is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. All therapeutic agents utilized with the EkoSonic® Endovascular System should be fully prepared and used according to the instruction for use of the specific therapeutic agent. ***Pulmonary Embolism:*** The EKOS EkoSonic® Endovascular System is intended for the treatment of pulmonary embolism patients with ≥ 50% clot burden in one or both main pulmonary arteries or lobar pulmonary arteries, and evidence of right heart dysfunction based on right heart pressures (mean pulmonary artery pressure ≥ 25mmHg) or echocardiographic evaluation.