

# CHEST<sup>®</sup> Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS



ROBERTO BADAGLIACCA, MD, PhD

Right heart catheterization allows only an indirect description of RV function, according to Dr. Badagliacca (center).

## ECHO, exercise testing reflect PAH prognosis

BY M. ALEXANDER OTTO  
Frontline Medical News

FROM CHEST

**A**dding echocardiography and cardiopulmonary exercise testing to baseline right heart catheterization improves prognostic accuracy in idiopathic pulmonary arterial hypertension, according to a prospective Italian study of 102 newly diagnosed patients.

A combination of low right ventricular fractional area change (RVFAC) on echocardiography and low oxygen pulse on cardiopulmonary exercise testing (CPET) “identifies patients at a particularly high risk of clinical deterioration.” Both are markers of right ventricular

(RV) function, which is a major determinant of outcome in idiopathic pulmonary arterial hypertension [iPAH], said investigators led by Roberto Badagliacca, MD, of the Sapienza University of Rome (Chest. 2016 Aug 20. pii: S0012-3692(16)56052-8. doi: 10.1016/j.chest.2016.07.036).

PAH diagnosis requires right heart catheterization, and findings have long been known to predict PAH outcome. However, catheterization allows only “an indirect description of RV function,” the investigators said. Recent studies have shown that RV echocardiography and CPET improve the accuracy of heart failure prognosis, so the investiga-

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## GOLD uncouples spirometry from ABCD algorithm

Guidance gives symptoms more weight

BY M. ALEXANDER OTTO  
Frontline Medical News

**T**he Global Initiative for Chronic Obstructive Lung Disease (GOLD) has uncoupled spirometry results from the ABCD treatment algorithm; this move marks the organization’s first announcement of major COPD guidance since 2011.

Spirometry now stands apart from GOLD’s ABCD symptom/exacerbation risk score with its own grade, with possibilities ranging from 1 to 4. A forced expiratory volume in 1 second (FEV<sub>1</sub>) of 80% or more of

the predicted value rates a 1; the score degrades to 4 with an FEV<sub>1</sub> below 30%.

GOLD had been moving toward symptoms and exacerbations to guide treatment for several years before formalizing the break from spirometry in its Nov. 16 report.

“In previous GOLD documents, recommendations for management of COPD were based solely on spirometric category. However, there is considerable evidence that the level of FEV<sub>1</sub> is a poor descriptor of disease status, and, for this reason, the management of stable COPD based on ...

See **GOLD** • page 4

## Blood pressure rose after CPAP halt

BY JIM KLING  
Frontline Medical News

FROM CHEST

**C**ontinuous positive airway pressure (CPAP) therapy for obstructive sleep apnea (OSA) has a significant beneficial effect on blood pressure, according to an analysis of participants in three randomized controlled trials.

Previous meta-analyses suggested that CPAP treatment led to an average of improvement of 2-3 mm Hg, but the estimates relied on heterogeneous trials that often had low levels of CPAP adherence, and those factors might have led to an underestimation of the treatment effect. The new analysis showed that halting CPAP increases

blood pressure between 5.0 and 9.0 mm Hg, compared with patients who continued using CPAP (Chest. 2016;150[6]:1202-10).

To get around the problem of adherence, researchers led by Malcolm Kohler, MD, at University Hospital of Zürich analyzed the results of three previous studies looking at the effects

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## Symptoms can guide treatment

**GOLD** *from page 1*

disease impact (determined mainly by symptom burden and activity limitation) and future risk of disease progression (especially of exacerbations) is recommended. ... ABCD groups

are now proposed to be derived exclusively from patient symptoms and their history of exacerbations," GOLD said.

The clear focus on symptoms and

exacerbations is "the major accomplishment" of the new report, which has been downloaded more than 45,000 times since its release, a testament to GOLD's importance to clinicians trying to help COPD patients.

"We are trying to do a better job of personalizing treatment," said GOLD board member Gerard Criner, MD,

FCCP, chair and professor of thoracic medicine and surgery at Temple University in Philadelphia.

The change "allows you to plan treatment based on symptoms [even] if you don't have immediate access to spirometry, and then refine treatment once you have spirometry results. It also allows you to escalate and

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deescalate treatment because you are not boxed into a letter grade group” forced by spirometry. “You can also take a better look at pharmacologic versus nonpharmacologic therapy” when deciding what to do, he said.

In short, “we think it gives more freedom” to manage patients based on what seems best, Dr. Criner said.

### The change allows you to plan treatment based on symptoms and then refine treatment once you have spirometry results, Dr. Criner noted.

GOLD included an example of how the new assessment can help. “Consider two patients,” it said, both with an  $FEV_1$  less than 30% and a COPD Assessment Test result of 18,

but one with no exacerbations in the past year and the other with three. Both would have scored a GOLD D in the old system, and been treated similarly.

“However, with the new proposed scheme, the subject with three exacerbations ... would be labeled GOLD [spirometry] grade 4, group D,” and their treatment would focus on exacerbations. The no-exacerbation patient would be classified as GOLD grade 4, group B. Treatment would focus on symptoms. Drugs are still an option, but also lung volume reduction and lung transplant, GOLD said. Spirometry, in other words, is

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Dr. Gerard J. Criner

less important than how the patient is doing.

The group incorporated “every major study up to the first week of November” in the new report, Dr. Criner said, so there’s more to consider.

For instance, it’s clear now that patients benefit from home oxygen if they are severely hypoxemic while sitting on the couch watching TV, but not if they desaturate only when they get up and walk around, or come into the clinic to exercise. “We did not” know that in 2011, he said.

GOLD also recommended pulmonary rehabilitation and palliative care when indicated, as well as ongoing evaluation to make sure patients are

*Continued on following page*

#### VIEW ON THE NEWS

**Vera De Palo, MD, FCCP, comments:** As health care moves toward individualized care plans for patients, the updated GOLD recommendations enhance the possibility of personalized COPD treatment. This means more

symptom-focused treatment for patients and, as Dr. Criner points out, more freedom for providers to manage patients based on what seems best.





Continued from previous page

able to use their inhalers, a major problem in COPD.

GOLD said that group A patients - those with few symptoms and low exacerbation risk - should be offered

**The guidance “allows you to escalate and deescalate treatment because you are not boxed into a letter grade group” forced by spirometry ... “[We] think it gives more freedom,” Dr. Criner noted.**

a bronchodilator. Initial therapy for group B - more symptoms, but low exacerbation risk - and group C - higher exacerbation risk but fewer symptoms - “should consist of a

single long-acting bronchodilator. There is no evidence to recommend one class of long-acting bronchodilator over another.”

For group D - highly symptomatic with frequent exacerbations - “we recommend starting therapy with a [long-acting beta-2 agonist]/[long-acting antimuscarinic antagonist] combination,” the group said.

There was no industry involvement in GOLD’s report, but numerous authors and board members had pharmaceutical company ties, and GOLD’s treatment advice relies on drug company studies. Dr. Criner reported personal payments from Holaria, and research funding and other nonpersonal payments from AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline, Johnson and Johnson, and others.

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## RVFAC outperformed other metrics

PAH from page 1

tors wanted to see if they’d do the same for PAH.

The results “strongly suggest that noninvasive measurements related to RV function obtained by combining resting echocardiography and CPET are of added value to right heart catheterization in the assessment of severity and prognosis of PAH,” the researchers said.

During a mean follow-up of 528 days, 54 patients (53%) had clinical worsening, defined as a 15% reduction in 6-minute walk distance from baseline plus a worsening of functional class, nonelective PAH hospitalization, or death.

Baseline functional class and cardiac index proved to be independent predictors of clinical worsening. Adding echocardiographic and CPET variables independently improved prognostic power (area under the curve, 0.81 vs. 0.66;  $P = .005$ ).

Compared with patients with high RVFAC and high oxygen pulse at baseline, patients with low RVFAC and low oxygen pulse had a 99.8 increase in the hazard ratio for clinical worsening, and those with high RVFAC and low oxygen had a 29.4 increase ( $P = .0001$ ).

Several echocardiographic variables for RV function have previously been reported as independent predictors of PAH outcome. “The new finding here is that RVFAC outperformed

other echocardiographic indices of systolic function,” the investigators wrote.

“As for peak oxygen pulse, this variable is thought to assess maximum [stroke volume],” assumed to be determined by RV function; MRI-determined stroke volume has been previously shown to be an important predictor of survival in PAH,” they said.

The mean age in the study was 52 years, mean functional class was 2.7, and mean 6-minute walk distance was 430 m; 62 subjects were women. The most relevant comorbidities were diabetes in 5 patients, hypercholesterolemia in 10, thyroid diseases in 6, and clinical depression in 7.

Patients with severe tricuspid regurgitation or exercise-induced opening of the foramen ovale were excluded. However, a reanalysis including patients with exercise-induced right to left shunting showed the same independent predictors of PAH outcome.

After diagnosis, patients were treated with endothelin receptor antagonists, phosphodiesterase-5 inhibitors, and prostanoids.

Dr. Badagliacca reported speaker and adviser fees from United Therapeutics, Dompe, GSK, and Bayer. His colleagues reported no conflicts of interest.

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

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# Adaptive servo ventilation cuts atrial fib burden

BY MITCHEL L. ZOLER  
*Frontline Medical News*

ORLANDO – Adaptive servo ventilation produced a significant and clinically meaningful reduction in atrial fibrillation burden in patients with heart failure and sleep apnea in results from an exploratory, prospective, randomized study with 35 patients.

Adaptive servo ventilation (ASV) “may be an effective antiarrhythmic treatment producing a significant reduction in atrial fibrillation without clear evidence of being proarrhythmogenic,” Jonathan P. Piccini, MD, said at the annual scientific meeting of the Heart Failure Society of America. “Given the potential importance of this finding further studies should validate and quantify the efficacy of ASV for reducing atrial fibrillation in patients with or without heart failure.” This is “the first time” the arrhythmia effects of a sleep apnea intervention, in this case ASV, was studied in a prospective, randomized way while using implanted devices to measure the antiarrhythmic effect of the treatment, said Dr. Piccini, an electrophysiologist at Duke University in Durham, N.C., in an interview.

The new finding means that additional, larger studies are now needed, he said.

The CAT-HF (Cardiovascular Improvements With Minute Ventilation-Targeted ASV Therapy in Heart Failure) trial was originally designed to randomize 215 heart failure patients with sleep disordered breathing – and who were hospitalized for heart failure – to optimal medical therapy with or without ASV at any of 15 centers in the United States and

Germany. But in August 2015, results from the SERVE-HF (Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure) trial, which generally had a similar design to CAT-HF, showed an unexpected danger from ASV in patients with central sleep apnea and heart failure with reduced ejection fraction (N Engl J Med. 2015 Sept 17;373[12]:1095-105). In SERVE-HF, ASV was associated with significant increases in all-cause and cardiovascular mortality. As a result, enrollment into CAT-HF stopped prematurely with just 126 patients entered, and ASV treatment of patients already enrolled came to a halt.

The primary endpoint in the underpowered and shortened CAT-HF study, survival without cardiovascular hospitalization and with improved functional capacity measured on a 6-minute walk test, showed similar outcomes in both the ASV and control arms. But in a prespecified subgroup analysis by baseline ejection fraction, the 24 patients with heart failure with preserved ejection fraction (19% of the CAT-HF enrollment) showed a statistically significant, 62% relative improvement in the primary endpoint linked with ASV treatment compared with similar patients who did not receive ASV, Christopher M. O'Connor, MD, professor of medicine at Duke University, reported in May 2016 at the European Heart Failure meeting in Florence.

Dr. Piccini's report focused on a prespecified subgroup analysis of CAT-HF designed to examine the impact of ASV on arrhythmias. As-

essment of the impact of ASV on atrial fibrillation was possible in 35 of the 126 patients in CAT-HF who had an implanted cardiac device (pacemaker, defibrillator, or cardiac resynchronization device) with an atrial lead, and assessment of ventricular arrhythmias occurred in 46 of the CAT-HF patients with an implanted high-voltage device (a defibrillator or resynchronization device) that allowed monitoring of ventricular arrhythmias.

For the atrial fibrillation analysis, the 35 patients averaged 60 years of age, and about 90% had a reduced ejection fraction. About two-thirds had an apnea-hypopnea index greater than 30.

The results showed that the 19 patients randomized to receive ASV had an average atrial fibrillation burden of 30% at baseline that dropped to 14% after 6 months of treatment. In contrast, the 16 patients in the control arm had a AF burden of 6% at

baseline and 8% after 6 months. The between-group difference for change in AF burden was statistically significant, Dr. Piccini reported, with a burden that decreased by a relative 21% with ASV treatment and increased by a relative 31% in the control arm. Analysis of the ventricular arrhythmia subgroup showed that ASV had no statistically significant impact for either lowering or raising ventricular tachyarrhythmias or fibrillations.

The CAT-HF trial was funded by ResMed, a company that markets adaptive servo ventilation equipment. Dr. Piccini has received research support from ResMed and from Janssen, Gilead, St. Jude, Spectranetics, and he has been a consultant to Janssen, Spectranetics, Medtronic, GSK and BMS-Pfizer. Dr. O'Connor has been a consultant to ResMed and to several other drug and device companies.

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## VIEW ON THE NEWS

**Krishna Sundar, MD, FCCP, comments:** A small prespecified subgroup of patients in the CAT-HF (Cardiovascular improvements with minute ventilation-targeted ASV therapy in heart failure) trial randomized to adaptive servo ventilation (ASV) showed a 21% relative reduction in atrial fibrillation burden as compared to the control arm which had only 31% relative reduction. While the CAT-HF study was discontinued following results of SERVE-



HF trial, this subgroup analysis included 35 patients (19 ASV arm; 16 control arm), the majority of whom had a reduced ejection fraction. This report poses interesting questions about effects of ASV on atrial fibrillation burden in those with reduced EF given the finding that central sleep apnea and Cheyne-Stokes respiration are shown to be associated with incident atrial fibrillation in older men (May et al. Am J Respir Crit Care Med 2016).

## Established CPAP users studied

Blood Pressure from page 1

of CPAP withdrawal. The analysis included 153 OSA patients on CPAP therapy, who had been randomized to continue therapy or to withdraw from therapy for 2 weeks. Eighty-seven of these patients discontinued CPAP, and the remaining 66 patients continued the therapy. Blood pressure was measured at home and in hospital.

On average, those who discontinued CPAP had an increase in office systolic blood pressure of 5.4 mm Hg (95% confidence interval, 1.8-8.9 mm Hg;  $P = .003$ ) and an increase in home systolic blood pressure of

9.0 mm Hg (95% CI, 5.7-12.3 mm Hg;  $P$  less than .001), compared with patients who continued CPAP. The effects of stopping CPAP, instead of continuing the therapy, on office diastolic blood pressure and home diastolic pressure were increases of 5.0 mm Hg (95% CI, 2.7-7.3 mm Hg;  $P$  less than .001) and 7.8 mm Hg (95% CI, 5.6-10.0 mm Hg;  $P$  less than .001), respectively.

Patients who discontinued CPAP also experienced a significant increase in apnea-hypopnea index, from 2.8/h to 33.2/h, while those who continued using CPAP, on average, experienced

only a 0.3/h increase in apnea-hypopnea index from baseline.

“One clinical implication is that if you do not need to stop CPAP for obstructive sleep apnea, do not stop it. This study also suggests the importance of monitoring your blood pressure in a home setting, under usual conditions,” summed up Robert Kloner, MD, PhD, director of the Huntington Medical Research Institutes Cardiovascular Research Lab, Pasadena, Calif., who was not involved in the study.

Previous studies of CPAP, such as the SAVE study published in the New England Journal of Medicine in September (N Engl J Med. 2016;375:919-31), often find little or no connection between CPAP ther-

apy and cardiovascular outcomes. That is probably because of inadequate adherence to CPAP therapy. “That’s always been the bane of sleep apnea studies,” said Krishna M. Sundar, MD, FCCP, who also did not participate in the study.

The current work got around the problem by looking at patients who had already established use of CPAP. “This is a very good study,” said Dr. Sundar, who is the medical director of the Sleep-Wake Center at the University of Utah, Salt Lake City.

The study was funded by the Swiss National Science Foundation and the University of Zürich. The analysis’ authors and the outside experts quoted in this story reported no financial disclosures.



# Failure of AEC2s implicated in pulmonary fibrosis

BY MARY ANN MOON  
*Frontline Medical News*

**T**he failure of type 2 alveolar epithelial cells (AEC2s), which are critical to the repair and regeneration of lung tissue, appears to be a major cause of pulmonary fibrosis, according to a report published online in *Nature Medicine*.

Researchers performed a series of in vitro and murine studies to better understand the molecular mechanisms underlying pulmonary fibrosis, which is believed to result from repeated microinjuries to the alveolar epithelium that in turn promote excessive, sustained fibroblast activation with matrix-producing myofibroblasts. They found that expression of both hyaluronan (HA) and Toll-like receptor 4 (TLR4) on AEC2s is deficient in a mouse model of pulmonary fibrosis and in samples of lung tissue from patients with the disease, but not in samples from healthy control subjects or from patients with chronic obstructive pulmonary disease (COPD).

"The main finding here is that the endogenous matrix glycosaminoglycan HA and the innate immune re-

ceptor TLR4 are required for optimal AEC2 renewal and for limiting fibrosis after lung injury," said Carol Liang, MD, of the department of medicine and the Women's Guild Lung Institute, Cedars-Sinai Medical Center, Los Angeles, and her associates.

"These findings are the first published evidence that pulmonary fibrosis is primarily a disease of AEC2

**"The main finding here is that the endogenous matrix glycosaminoglycan HA and the innate immune receptor TLR4 are required for optimal AEC2 renewal and for limiting fibrosis after lung injury," Dr. Liang said.**

stem cell failure," Dr. Liang said, in a written statement.

The investigators began by showing that AEC2s engineered to stop expressing hyaluronan or TLR4 (by deleting the genes that encode for that expression) showed impaired self-renewal in vitro, compared with normal AEC2s. In a mouse model,

the engineered AEC2s also caused impairment in the healing of deliberately induced lung injury.

In addition, the researchers developed a mouse model of pulmonary fibrosis and showed that treatment with exogenous interleukin 6 "enhanced AEC2 renewal and partially reversed the fibrotic phenotype" in vivo.

"To determine whether our observations in the mouse model of [deficient] AEC2s have relevance to human disease, we isolated AEC2s from lung explants of human subjects who had undergone lung transplantation because of [idiopathic pulmonary fibrosis]," the researchers said. These samples showed marked depletion in the number of AEC2s, compared with samples taken from healthy control subjects and from patients with COPD.

In addition, the few remaining AEC2s in the samples affected by pulmonary fibrosis were deficient in the expression of HA, compared with those in the samples from control subjects. This suggests that loss of cell-surface HA is unique to severe pulmonary fibrosis, the researchers said (*Nature Med.* 2016. doi: 10.1038/

nm.4192).

Since pulmonary fibrosis is characterized by patchy areas of parenchymal fibrosis alternating with relatively normal lung tissue, the investigators then compared AEC2s taken from these two distinct types of tissue in the patient group. They found that AEC2 cells from affected areas of the lung showed much more markedly reduced expression of HA than those from healthy areas of the lung. Flow cytometry testing further demonstrated that the number of AEC2s also was greatly reduced in affected lung tissue but relatively higher in more normal lung tissue. However, even the "healthy" lung tissue from affected patients had lower numbers of AEC2s and impaired cell renewal when compared with tissue from unaffected control subjects, the researchers noted.

"In future studies, we will explore how the loss of hyaluronan promotes fibrosis and how it might be restored to cell surfaces. These endeavors could lead to new therapeutic approaches" for this progressive, fatal disease for which there is no effective treatment at present, Dr. Liang said, in the written statement.

## Severe post-thoracotomy pain predicts persistent postop pain

BY DEEPAK CHITNIS  
*Frontline Medical News*

**P**atients who suffer from severe pain in the days immediately following an open thoracotomy are significantly more likely to still be experiencing pain from the procedure 6 months later, according to a study published in the *Journal of Clinical Anesthesia*.

"A recognized cause of persistent postsurgical pain is poorly controlled immediate postoperative pain," wrote the authors, led by Gopinath Niraj, MD, of the University Hospitals of Leicester (England) NHS Trust. "Open thoracotomy can induce significant pain during the immediate postoperative period. Patients undergoing thoracotomy also have one of the greatest incidences of chronic postoperative pain and disability among all the surgical procedures."

The researchers gave a questionnaire to 504 patients who underwent open thoracotomy at a single center between May 2010 and April 2012. They asked yes/no questions about the existence of and location

of postoperative pain, and numerical questions regarding the severity of pain. Scores of 7 or higher on a 10-point scale indicated "severe pain," according to the investigators (*J Clin Anesth.* 2017;36:174-7). Subjects were evaluated at 72 hours and at 6 months after the operation.

Of the 504 patients, there were 364 survivors, of which 306 received questionnaires. Of those 306, 133 (43%) reported at least five incidents of severe pain within 72 hours of undergoing the operation. Within this group, 109 (82%) reported feeling some amount of persistent pain 6 months later. Chronic post-thoracotomy pain was considered severe in 10% of those subjects, while 24% reported it as moderate and 48% said it was mild. A total of 289 of the 306 subjects (95%) received an epidural analgesic in the 72 hours after thoracotomy. Pain management was rated excellent by 36.3%, good by 43.8%, fair by 15.8%, and poor by 3.8% of patients.

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## Two factors associated with vocal cord dysfunction in study

BY DOUG BRUNK  
*Frontline Medical News*

AT CHEST 2016

LOS ANGELES – Female sex and the absence of wheezing were the only factors significantly associated with vocal cord dysfunction in patients with high pretest probability of disease, a retrospective analysis showed.

The findings differ from those of the Pittsburgh Vocal Cord Index, which identified symptoms of throat tightness, dysphonia, absence of wheezing, and the presence of odors as key features predictive of vocal cord dysfunction (VCD). "This proves the point that VCD is an elusive diagnosis," lead study author Phalgun Shah, MD, said, in an interview, at the annual meeting of the American College of Chest Physicians. "If you have a high rate of clinical suspicion, you don't have to do a laryngoscopy. Send them for speech therapy. If they get better, they have VCD."

Of 244 patients who Dr. Shah and his colleagues retrospectively evaluated, 136 (56%) were diagnosed with VCD; the remaining 108 (44%) were

not. As many as 66% of females had a diagnosis of VCD, compared with 48% of males ( $P = .006$ ). The percentage of patients with VCD who had an absence of wheezing was 49% ( $P = .037$ ).

Depression, anxiety, throat tightness, dysphonia, odor symptom trigger, lack of response to bronchodilator or truncation, and flattening of the inspiratory volume curve did not predict VCD.

The patients were active duty military personnel and veterans who were referred to the pulmonary function lab at Tripler Army Medical Center, Honolulu, for suspected VCD between 2010 and 2014. The researchers identified patients by laryngoscopy procedure code and collected numerous variables, including demographic information, past medical history, pulmonary function test data, and clinical variables such as ED visits for dyspnea. "For the first time, we are saying that exercise laryngoscopy is not the gold standard," said Dr. Shah of the division of pulmonary and critical care at Tripler.

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# 'Stepping' up robotic lobectomy instruction

BY RICHARD MARK KIRKNER  
*Frontline Medical News*

Teaching minimally invasive robotic surgery to residents can be difficult in a health care environment obsessed with quality outcome measures and under scrutiny by hospital administrators and payers, but researchers at the University of Alabama at Birmingham may have devised a method to instruct residents in robotic lobectomy without compromising patient outcomes, according to a study published in the October issue of the *Journal of Thoracic and Cardiovascular Surgery* (2016;152:991-7).

Robert J. Cerfolio, MD, MBA, FCCP, and his co-authors divided the procedure into 19 sequential, teachable steps and allowed residents to perform selected steps during operations that Dr. Cerfolio directed.

"We then applied simulation training, coaching techniques, and video

review of each step to help improve the steps that residents could not complete," Dr. Cerfolio and his coauthors said.

Surgeons in academic centers face the challenge of teaching "the art and science of surgery," Dr. Cerfolio and his colleagues said, while maintaining quality outcomes. "Teaching minimally invasive surgery, especially robotic surgery, is challenging given the risks and the limited availability of the robot."



DR. CERFOLIO

The researchers acknowledged that other groups have taken a similar approach to training, but this is the first study that included video review, coaching, and instruction tied to time constraints, they said.

"A major concern is that while teaching robotic surgery, patients can be injured, care is worse, and metrics that are increasingly used as surrogates for quality outcomes suffer," they noted.

They allotted each step in the procedure a set amount of time in which the resident had to complete

it, totaling 80 minutes for all 19 steps and ranging from 1 minute to inspect the pleura after placing ports (9 minutes) to 20 minutes to close the five incisions. If the resident completed the task in the allotted time, it was recorded as "performed."

Between February 2010 and December 2010 Dr. Cerfolio performed 520 robotic lobectomies, and over time the percentage of successful steps per resident improved.

For example, in the first year, 50% of thoracic surgery residents completed the first five steps (mark and place ports, inspect pleura, resect the inferior pulmonary ligament, and remove three lymph nodes), but by the last year of the study 90% of them successfully completed the five steps.

Dr. Cerfolio and coauthors acknowledged "many flaws" in their study, but the study also had strengths: It involved only one operation and corroborated the database with each resident's own surgical logs.

"Operations such as robotic lobectomy can be successfully taught by dividing them into a series of surgical

## VIEW ON THE NEWS

**Francis J. Podbielski, MD, FCCP, comments:** This is an interesting and clinically relevant study given the emphasis many institutions have placed on becoming "robotic" centers of excellence. The overall cost effectiveness of robotic surgery from a public policy standpoint remains a matter of intense study given the scarcity of resources in many health-care settings.

noted. Recording what residents can and can't do, reviewing video, and coaching contribute to the process to improve their skills. "Further studies that scientifically measure 'ways to teach' and ways to coach and mentor are needed," they said.

Dr. Cerfolio disclosed relationships with Intuitive Surgical, Ethicon, Community Health Services, KCL, Bovie and C-SATS. Co-author Douglas Minnich, MD, is a consultant to Medtronic. The other co-authors had no financial relationships to disclose.

# REBOA may be thoracotomy alternative in traumatic arrest

BY JESSICA CRAIG  
*Frontline Medical News*

WASHINGTON – Resuscitative endovascular balloon occlusion of the aorta (REBOA) could be an acceptable alternative to thoracotomy in traumatic arrest patients who are hemorrhaging below the diaphragm, according to the results of a small pilot study which were presented by William Teeter, MD, at the annual clinical congress of the American College of Surgeons.

Furthermore, virtual simulation training sufficiently prepares surgeons to safely use the REBOA technique in the acute care setting, a separate study found. Importantly, this training has the potential to allow REBOA to become a widespread tool for surgeons regardless of their endovascular surgical experience.

REBOA is an emerging and less invasive method of aortic occlusion during traumatic arrest. "Recent evidence published in the *Journal of Trauma* suggests that REBOA has similar outcomes to resuscitative thoracotomy with aortic cross-clamping or RTACC," said Dr. Teeter, who is currently an emergency medicine resident at the University of North Carolina, Chapel Hill, but conducted this research during a fellowship at the University of Maryland Medical Center's R Adams Cowley Shock Trauma Center in Baltimore.

Dr. Teeter presented the preliminary results of a pilot study involving 19 patients who received RTACC between 2008 and 2013 and 17 patients who received REBOA between 2013 and 2015. All study

participants were trauma patients who arrived at the R Adams Cowley Shock Trauma Center in arrest or arrested shortly after arrival.

Age, gender, Glasgow Coma Scale, and injury severity score were the same or similar between the two groups, Dr. Teeter reported. Mean systolic blood pressure at admission was 14 mmHg for

**"At our center there has been a marked change in practice regarding which patients receive resuscitative thoracotomy and which get REBOA," said Dr. William Teeter.**

the REBOA group and 28 mmHg for the RTACC group; however, the majority of patients (82% of REBOA patients and 73% of RTACC patients) arrived with a blood pressure of 0, reported Dr. Teeter.

Importantly, patients in the RTACC group who had penetrating chest injury were excluded for this analysis, Dr. Teeter noted, adding that there was a slightly higher incidence of blunt trauma within the REBOA group likely due to "a change in practice at the trauma center during this time."

All resuscitations were captured with real-time videography. Continuous vitals were also collected and analyzed.

While more RTACC patients survived to the

operating room (53% vs. 68%), among the REBOA group there were more patients who experienced return of spontaneous circulation (53% vs. 37%). However, neither of these results was statistically significant.

Following occlusion of the aorta, the blood pressure measures, taken from continuous vital signs and averaged over a 15-minute period, were 80 mmHg for the REBOA group and 46 mmHg for the RTACC group. Again, this result was statistically insignificant but trended toward favoring REBOA.

Overall, patient survival was dismal. Only one patient who received REBOA survived.

Following Dr. Teeter's presentation, the study's assigned discussant, Nicole A. Stassen, MD, of the University of Rochester Medical Center, N.Y., noted that while post-occlusion blood pressure was higher for the REBOA group it seemed not to matter as the majority of patients did not survive. Dr. Stassen also asked if these preliminary results were sufficient to inform or change clinical practice.

In response, Dr. Teeter explained that the pilot study was conducted at a time when the literature was unclear about how patients would respond to open versus endovascular occlusion, and this data helped guide further research and resuscitation efforts.

"At our center there has been a marked change in practice regarding which patients receive resuscitative thoracotomy and which get REBOA," he added and concluded that "these and previous data

*Continued on page 16*

# Cerebral protection in TAVI cuts ischemic lesions

BY MARY ANN MOON  
Frontline Medical News

In patients undergoing transcatheter aortic valve implantation, use of a cerebral protection device to entrap and remove embolic debris reduced both the number and the size of ischemic brain lesions, according to a report published in JAMA.

The frequency and severity of post-procedure stroke symptoms were similar with and without the filter; however, the researchers noted that the study included only 100 patients and was not powered to assess differences in stroke rates.

Various cerebral protection devices were invented in response to the finding of a threefold increase in periprocedural stroke mortality following TAVI. Yet “clear evidence of the efficacy of any embolic protection device in TAVI is still missing,” said Stephan Haussig, MD, of the University of Leipzig (Germany) Heart Center, and his associates.

They performed a prospective randomized clinical trial at their center to assess the efficacy of the only cerebral protection device that was available when their study was designed. For the study, 100 patients with severe, symptomatic aortic stenosis were randomly assigned to undergo TAVI either with (50 patients) or without (50 patients) the use of a protective filter to capture embolic debris. The filter device was estimated to fully protect 74% of the brain and partially protect 24%, leaving only 2% unprotected.

The primary endpoint of the study was the number of ischemic brain lesions detected on diffusion-weighted MRI in the filter group, compared with the control group. This imaging was performed at baseline, 2 days after the procedure, and 7 days after the procedure.

In protected brain regions, the median number of new ischemic

**It is important to note that this study wasn't powered to assess differences in stroke rates. Larger studies will need to be completed to assess the impact of protective devices on neurological and functional outcomes, according to Dr. Stephan Haussig and his associates.**

brain lesions was markedly lower in the filter group than in the control group (4 vs. 10) at 2 days, as well as at 7 days (3 vs. 7, respectively). In addition, the volume of new lesions in protected brain regions also was markedly lower in the filter group at 2 days (242 mm vs. 527 mm) and at 7 days (101 mm vs. 292 mm).

Similar protective effects were evident when the entire brain was evaluated. The median number of new lesions was markedly lower in the filter group than in the control group (8 vs. 16) at 2 days and at 7 days (5 vs. 10, respectively). The median lesion

volume also was markedly lower in the filter group at 2 days (466 mm vs. 800 mm) and at 7 days (205 mm vs. 720 mm).

However, this protective effect didn't translate into a substantive difference in neurologic outcomes between the two study groups, as assessed by the National Institutes of Health Stroke Scale and the modified Rankin scale. Five patients in each group developed symptoms of stroke, and all symptoms were deemed minor and nondisabling, the investigators said (JAMA 2016;316[6]:592-601).

It is important to note that this study wasn't powered to assess differences in stroke rates. Larger studies will be needed to assess the impact of protective devices on neurological and functional outcomes, Dr. Haussig and his associates wrote.

The two study groups also did not differ with regard to complications. Thirty-day mortality was 0% in the filter group and 2% in the control group, a nonsignificant difference.

The investigators pointed out that protective filter devices can protect the brain only while they are in place during TAVI, “which usually takes less than 1 hour and represents only 2% of the first 48 hours after which the first MRI was performed in this study. Based on the analyzed material captured and removed by the filters – e.g., old and fresh thrombus, endothelium, atheromatous plaque, valve tissue, and calcium – it becomes evident that causes of cerebral injury are

## VIEW ON THE NEWS

**Hossein G. Almassi, MD, FCCP, comments:** As there was no significant difference in clinical neurological outcomes related to use of a filter device, although there was significantly fewer and smaller brain lesions in the stroke group, one is left to conclude that the majority of MRI findings after TAVI are not clinically relevant. Is the added cost of a cerebral protection device cost effective given the equivalent neurological outcomes in the both groups?

risk does not resolve immediately at the end of the TAVI procedure,” they said.

Perhaps the study's most surprising finding was that nearly every patient had new cerebral lesions consistent with infarcts, but most of these were very small and not associated with any neurocognitive or functional impairments.

This study was limited in that it involved a single cardiac team assessing only one brand of filter device at a single hospital, so the results are not necessarily generalizable to a broader patient population or to the many other devices that have since been developed, Dr. Haussig and his associates added.

This study was funded by a grant from Claret Medical and Medtronic. Dr. Haussig reported having no relevant financial disclosures; his associates reported ties to numerous industry sources.

*Continued from page 11*

suggest that the time performing thoracotomy for resuscitation purposes may be better spent performing CPR with REBOA.”

At the very least, this pilot study demonstrated that “REBOA may be an acceptable alternative to RTACC.” Further analysis of larger study populations will be published soon and will show that REBOA may be preferred over RTACC, according to Dr. Teeter.

In a subsequent presentation, David Hampton, MD, a surgical critical care fellow at the University of Maryland Medical Center's R Adams Cowley Shock Trauma Center, confirmed that many recent studies have demonstrated that REBOA is a comparable alternative to emergency thoracotomies. In fact, REBOA is commonly used throughout Japan, the United Kingdom, and in northern Europe; however, in the United States, REBOA is currently only used at a few Level 1 trauma centers and in the military, according to Dr. Hampton.

A major hindrance to wider-spread REBOA use

in the United States is the lack of endovascular training for surgeons during residency which has resulted in a limited number of surgeons who can perform the REBOA technique and a limited number of surgeons who can teach the procedure to others, said Dr. Hampton.

In lieu of experience, formalized 1- or 2-day endovascular simulation courses, such as BEST, were created to prepare surgeons to use techniques such as REBOA. Prior validation studies, including those conducted by researchers at the University of Maryland, demonstrated that surgeons who participated in these courses improved surgical technique and increased their surgical knowledge base, Dr. Hampton reported.

To further elucidate the benefits of these training courses on the successful use of REBOA in the acute care setting, Dr. Hampton and his associates selected nine acute care surgeons with varying endovascular surgical experience to complete the 1-day BEST course and then compared surgeons' performances of the REBOA technique after successful course completion.

During the study, a total of 28 REBOA procedures were performed, 17 by the surgeons with no endovascular experience, and the remaining 11 by surgeons with endovascular surgical experience.

Overall, there was no difference in wire placements, sheath insertion, position or localization of balloons, or balloon inflation. In addition, there was no difference in mortality among patients, and there were no known REBOA complications during this study.

In conclusion, endovascular experience during residency is not a prerequisite for safe REBOA placement, Dr. Hampton commented.

Taken together, these two research studies are really helping to break ground on REBOA use in the acute care setting, commented an audience member.

The Department of Defense funded Dr. Teeter's study. Dr. Teeter and Dr. Hampton both reported having no disclosures.

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# CSLap for post-esophageal surgery complications

BY RICHARD MARK KIRKNER  
*Frontline Medical News*

Ingestion of caustic substances like alkali, acid, and bleaches that call for esophageal surgery is relatively rare, and the study of dealing with postsurgery complications even rarer, but a team of surgeons from a large public referral hospital in Paris has collected enough cases over the first years of this century to report that a form of revision surgery in these cases can yield good outcomes with acceptable morbidity, according to a study in the *Journal of Thoracic and Cardiovascular Surgery* (2016;152:1378-85).

Thibault Voron, MD, and coauthors at Hôpitaux Saint-Louis and the University of Paris performed revision cervicosternolaparotomy (CSLap) on 55 patients from 1999 to 2015. Two patients (4%) died and the severe morbidity rate was 27%, but the long-term functional success rate was 85%. "Of note, these figures compare favorably with results of primary esophageal reconstruction for caustic injuries in the literature," Dr. Voron and colleagues said. Overall the study authors performed revision surgery on 100 patients, with the remaining 45 undergoing repair through a limited approach. There were no significant differences in characteristics between the two groups.

Primary esophageal reconstruction for caustic injuries can usually be done at referral centers with good results, but up to half of these patients can have late complications, consisting mostly of strictures and redundancy that can cause loss of function, Dr. Voron and coauthors said. Published series have reported revision surgery in 15%-38% of patients (*Dis Esophagus*. 2008;21:E1-5; *Dis Esophagus*. 1999;12:7-9), but revision surgery itself is difficult to accomplish.

CSLap involves a large operative field from the jaw to the pubis. It starts with a comprehensive neck exploration through the previous cervical incision or with a median laparotomy to rule out a limited-approach repair. CSLap was undertaken when the graft was too short for a tension-free anastomosis. After the upper part of the graft was dissected from the thoracic inlet, the abdomen was opened for dissection of the abdominal part of the transplant. All scar tissues and strictures were excised after the transplant release, and a new anastomosis was constructed in healthy tissues. In cases involving life-threatening complications,

patient survival prevailed over graft preservation and reconstruction of digestive continuity. The operations took up to 10 hours, with 8 hours, 20 minutes the median.

The researchers found 2 distinct in-

dications for CSLap: graft strictures in 43 (78%) of patients to rescue the primary conduit and reconstruct the cervical anastomosis and a need to access the retrosternal space to treat graft-related complications. "Graft lengthen-

ing was definitely not the issue in this situation," they said of the latter indication. Four patients had emergency revision CSLap for spontaneous graft perforation and complications related to caustic reingestion.



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# TAVR valve durability supported in follow-up

BY MITCHEL L. ZOLER  
*Frontline Medical News*

WASHINGTON – First-generation, balloon-expandable transcatheter aortic valves had a less than 1% rate of valve failure in planned echocardiography examinations during follow-up that extended as long as 5 years after valve placement in more than 2,400 patients, a demonstration of durability that experts uniformly called “reassuring.”

This finding from patients who underwent transcatheter aortic valve replacement (TAVR) in the first U.S. pivotal trial for these devices, PARTNER 1 parts A and B, and during the subsequent continued-access program at PARTNER 1 study sites, represents the largest and longest systematic ultrasound follow-up of TAVR patients, Pamela S. Douglas, MD, said at the Transcatheter Cardiovascular Therapeutics annual meeting.

This evaluation of 2,404 TAVR patients in the PARTNER 1 trial examined by echocardiography and encompassing 6,493 patient-years of follow-up is the “largest core-lab based study of transcatheter heart valves to date. These data demonstrate excellent durability of transcatheter heart valves, suggesting that the low 5-year survival observed in this cohort is not related to adverse hemodynamics or transcatheter heart valve deterioration,” said Dr. Douglas, professor of medicine at Duke University, Durham, N.C.

Her findings showed that out of the 2,482 patients treated with TAVR (and including those without echo follow-up) either in the trial or

during the continued access program and followed for a median of 2.9 years and an average of 2.6 years, 20 patients (0.8%) required a reintervention. Four of these 20 patients (0.2% of the total cohort) showed a “classic pattern” of aortic valve deterioration marked by an increased valve pressure gradient and a reduced valve area, she reported.

“Reintervention was rare, became less frequent over time, and was usually not due to structural deterioration of the transcatheter heart valve,” she said. But Dr. Douglas also cautioned that among the patients who received the first-generation, balloon expandable Sapien valve in this cohort, just 39% survived to 5 years, and a mere 282 patients (11%) actually underwent echocardiographic examination at 5 years.

“This is one of several steps we need to take to figure out the durability of transcatheter valves,” said Jeffrey J. Popma, MD, professor of medicine and an interventional cardiologist at Beth Israel Deaconess Medical Center, Boston. He noted that data are needed from follow-up periods of 8 or 10 years, but these data will not be available until intermediate- or low-risk patients undergo TAVR in controlled circumstances and have long-term follow-up.

“Ten-year follow-up data will essentially be impossible” for the high-risk or inoperable patients treated with TAVR in the PARTNER 1 trial, which focused on the sickest patients with aortic stenosis, said Dr. Popma, lead investigator for several studies of TAVR using self-expanding aortic valves and marketed as CoreValve devices.

“We obviously need to follow patients longer. The 5-year results look terrific, and so very reassuring, but we need to keep an eye on this as we move TAVR into less sick and younger patients,” said Dr. Robert O. Bonow, professor of cardiology at Northwestern University, Chicago. “Durability is the remaining frontier in terms of moving TAVR into younger patients,” Dr. Bonow said at the meeting, which was sponsored by the Cardiovascular Research Foundation.

These data continue to show that “transcatheter valves have looked hemodynamically superior to surgically-placed valves with respect to the VARC (Valve Academic Research Consortium)–2 criteria” for prosthetic valve function, Dr. Popma noted.

PARTNER 1 was sponsored by Edwards Lifesciences, the company that had marketed the Sapien first-generation, balloon expandable TAVR system. Dr. Douglas has received research support from Edwards. Dr. Popma has been the lead investigator for several studies of a self-expanding TAVR system sponsored by Medtronic, and he has also received research funding from several other companies, has been a consultant to Boston Scientific and Direct Flow, and owns equity in Direct Flow. Dr. Dvir has been a consultant to and received research support from Edwards, Medtronic, and St. Jude. Dr. Reardon has been a consultant to Medtronic.

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## Embolic protection cut lesions, did not aid neurocognition

BY MARY ANN MOON  
*Frontline Medical News*

The largest randomized clinical trial to assess the safety and efficacy of cerebral embolic protection systems during transcatheter aortic valve replacement yielded puzzling and somewhat contradictory results, according to a report presented at the Transcatheter Cardiovascular Therapeutics annual meeting and published simultaneously in the *Journal of the American College of Cardiology*.

Virtually every device in this industry-sponsored study involving 363 elderly patients (mean age, 83.4 years) with severe aortic stenosis trapped particulate debris as intended, the mean volume of new lesions in the protected areas of the brain was reduced by 42%, and the number and volume of new lesions correlated with neurocognitive outcomes at 30 days.

However, the reduction in lesion volume did not achieve statistical significance, and the improvement in neurocognitive function also did not reach statistical significance.

In addition, “the sample size was clearly too low to assess clinical outcomes, and in retrospect, was also too low to evaluate follow-up MRI findings or neurocognitive outcomes.” Nevertheless, the trial “provides reassuring evidence of device safety,” said Samir R. Kapadia, MD, of the Cleveland Clinic (J Am Coll Cardiol. 2016 Nov 1. doi: 10.1016/j.jacc.2016.10.023).

In this prospective study, the investigators assessed patients at 17 medical centers in the United States and 2 in Germany. In addition to being elderly, the study patients were at high risk because of frequent comorbidities, including atrial fibrillation (31.7%) and prior stroke (5.8%).

In all, 121 patients were randomly assigned to undergo TAVR with a cerebral embolic protective device and 119 to TAVR without a protective device. New brain lesions were then assessed via MRI at 2-7 days post procedure, and neurocognitive function was assessed at 30 days.

### VIEW ON THE NEWS

**Francis J. Podbielski, MD, FCCP, comments:** The authors have demonstrated the safety of cerebral protection systems, but not their clinical benefit in terms of preventing adverse neurological outcomes. As they note, a larger study group might produce a statistical difference. Commentary on the added cost of the device would be helpful to weigh their cost effectiveness.

went TAVR but not MRI in a safety arm of the trial.

The protection devices were placed “without safety concerns” in most patients. The rate of major adverse events with the device was 7.3%, markedly less than the 18.3% pre-specified performance goal for this outcome. Total procedure time was lengthened by only 13 minutes when the device was used, and total fluoroscopy time was increased by only 3 minutes. These findings demonstrate the overall safety of using the device, Dr. Kapadia said.

Debris including thrombus with tissue elements, artery wall particles, calcifications, valve tissue, and foreign materials was retrieved from the filters in 99% of patients.

The mean volume of new cerebral lesions in areas of the brain protected by the device was reduced by 42%, compared with that in patients who underwent TAVR without the protection device. However, this reduction was not statistically significant, so the primary efficacy endpoint of the study was not met.

Similarly, neurocognitive testing at 30 days showed that the volume of new lesions correlated with poorer outcomes. However, the difference in neurocognitive function between the intervention group and the control group did not reach statistical significance.

The 5-day “window” for MRI assessment having been too long was among the study’s limitations, Dr. Kapadia said.

Claret Medical funded the study and Dr. Kapadia’s associates reported numerous ties to industry sources. The meeting was sponsored by the Cardiovascular Research Foundation.



DR. KAPADIA

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# Introducing our new Editorial Board Members



**M. Patricia Rivera, MD, FCCP**, is a Professor of Medicine in the Pulmonary Division, Department of Medicine at the University of North Carolina at Chapel Hill. She is a Co-Director of the Multidisciplinary Thoracic Oncology Program, and Director of the Lung Cancer Screening Program at UNC. She currently serves as Co-chair of the CHEST Thoracic Oncology NetWork and has been an editor and writer for the CHEST Lung Cancer Guidelines.



**Nirmal S. Sharma, MD**, is an Assistant Professor of Medicine in the Division of Pulmonary, Allergy and Critical Care Medicine at the University of Alabama at Birmingham. His clinical expertise is in the field of lung transplantation and advanced lung diseases including extracorporeal life support technologies for acute respiratory failure. His research is focused on the interaction of lung microbiome and innate immunity and its role in causing chronic rejection in lung transplantation. His other clinical interests include management of acute respiratory distress syndrome, pulmonary embolism, and lung donor management.

## This month in *CHEST*: Editor's picks

BY RICHARD S. IRWIN, MD, MASTER FCCP

Editor in Chief, CHEST

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# SLEEP STRATEGIES: Sleep-disordered breathing and pregnancy complications: Emerging data and future directions

BY FRANCESCA FACCO, MD

## Background

Sleep-disordered breathing (SDB) conditions are characterized by abnormal respiratory patterns and abnormal gas exchange during sleep.<sup>1-3</sup> Obstructive sleep apnea (OSA), the most common type of SDB, is characterized by repetitive episodes of airway narrowing during sleep that lead to respiratory disruption, hypoxia, and sleep fragmentation. In reproductive-aged women, epidemiologic studies



DR. FACCO

suggest a 2% to 13% prevalence of OSA.<sup>4-6</sup> Pregnancy is associated with changes that promote OSA, such as weight gain and edema of the upper airway.<sup>7</sup> Frequent snoring, a common symptom of OSA, is endorsed by 15% to 25% of pregnant women.<sup>8-10</sup> Health outcomes that have been linked to SDB in the nonpregnant population, such as hypertension and insulin-resistant diabetes, have clinically relevant correlates in pregnancy (preeclampsia, gestational diabetes).<sup>11-13</sup> The underlying mechanistic pathways linking SDB and adverse pregnancy outcomes are likely multifactorial. SDB leads to oxidative stress, autonomic dysfunction, inflammation, endothelial damage, and altered hormonal regulation of energy expenditure.<sup>14</sup> These same biologic pathways have been linked to adverse pregnancy outcomes.<sup>15</sup>

While several retrospective and cross-sectional studies suggest that SDB may increase the risk of developing hypertensive disorders and gestational diabetes during pregnancy,<sup>16-18</sup> up until recently, there were limited and conflicting data from prospective observational cohorts in which SDB exposure and pregnancy outcomes have been methodically measured and confounding variables carefully considered.<sup>19-21</sup> Louis et al.<sup>19</sup> reported on a cohort of 175 obese women and demonstrated that women with SDB (apnea-hypopnea index greater than or equal to 5) were more likely to develop preeclampsia (adjusted odds ratio, 3.5; 95% CI, 1.3, 9.9). However, two other small studies failed to demonstrate a positive association between SDB and pregnancy-related hypertension, but one suggested a relationship between SDB and gestational diabetes.<sup>20,21</sup>

## Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be Sleep-Disordered Breathing Substudy

The Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be Sleep-Disordered Breathing Substudy (nuMoM2b-SDB) was a prospective cohort study.<sup>22,23</sup> Level 3 home sleep tests were performed using a six-channel monitor that was self-applied by the participant twice during pregnancy, first between 60 and 150 weeks of pregnancy and then again between 220 and 310 weeks. An apnea-hypopnea index (AHI) of at least 5 was used to define SDB. The study was powered to test the primary hypothesis that SDB occurring in pregnancy is associated with an increased incidence of preeclampsia. Secondary outcomes were rates of hypertensive disorders of pregnancy, defined as preeclampsia and prenatal gestational hypertension, and gestational diabetes. Crude and adjusted odds ratios and 95% confidence intervals were calculated from univariate and multivariate logistic regression models. Adjustment covariates included maternal age (less than or equal to 21, 22-35, and over 35 years), body mass index (less than 25, 25 to less than 30, greater than or equal to 30 kg/m<sup>2</sup>), chronic hypertension (yes, no), and, for midpregnancy, rate of weight gain per week between early and midpregnancy assessments, treated as a continuous variable.

There were 3,705 women enrolled. AHI data were available for 3,132 (84.5%) and 2,474 (66.8%) women in early and midpregnancy, respectively. The corresponding prevalence of SDB was 3.6% and 8.3%. The overall prevalence of preeclampsia was 6.0%; hypertensive disorders of pregnancy, 13.1%; and gestational diabetes, 4.1%. In early and midpregnancy, the adjusted odds ratios for preeclampsia when SDB was present were 1.94 (95% CI, 1.07-3.51) and 1.95 (95% CI, 1.18-3.23), respectively; hypertensive disorders of pregnancy, 1.46 (95% CI, 0.91-2.32) and 1.73 (95% CI, 1.19-2.52); and gestational diabetes mellitus, 3.47 (95%, CI 1.95-6.19) and 2.79 (95% CI, 1.63-4.77). Additionally, increasing exposure-response relationships were observed between AHI and both hypertensive disorders and gestational diabetes.<sup>23</sup>

## Conclusions and future directions

The nuMoM2b data are provocative because sleep apnea is a potentially modifiable risk factor for adverse pregnancy outcomes. While a majority of SDB

	Early Pregnancy (6-15 weeks)		Midpregnancy (22-31 weeks)	
	AHI < 5	AHI ≥ 5	AHI < 5	AHI ≥ 5
Preeclampsia	170/3017 (5.6)	16/114 (14.0)	114/2266 (5.0)	26/206 (12.6)
Hypertensive disorders of pregnancy	378/3017 (12.5)	28/114 (24.6)	266/2266 (11.7)	51/206 (24.8)
Gestational diabetes	107/2965 (3.6)	21/110 (19.1)	69/2231 (3.1)	27/201 (13.4)

cases identified during pregnancy were mild, the nuMoM2b data demonstrate that even modest elevations of AHI in pregnancy are associated with an increased risk of developing hypertensive disorders and an increased incidence of gestational diabetes.

Pregnancy is conceivably an ideal scenario in which to better understand the role of SDB treatment as a preventive strategy for reducing cardiometabolic morbidity as the time frame needed to measure incident outcomes after initiating therapy is significantly contracted. However, data regarding the role of OSA treatment with continuous positive airway pressure (CPAP) during pregnancy, both regarding its acceptability to patients and its therapeutic benefit, are extremely limited. Further research is needed to establish whether universal screening for and treating of SDB in pregnancy can mitigate the risks and consequences of hypertensive disorders of pregnancy and gestational diabetes. However, in the meantime, we have to recognize that as our obstetric patient population is becoming more obese, we will encounter more women with symptomatic SDB in pregnancy. It is well documented that patients with symptomatic SDB, those who report that their snoring leads to chronic sleep disruption and excessive daytime sleepiness, can benefit from CPAP in terms of sleep quality and daytime function. Therefore, in addition to encouraging women already prescribed CPAP to continue their therapy during pregnancy, obstetricians who encounter a patient reporting severe SDB symptoms should refer her to a sleep specialist for further evaluation.

*Dr. Facco is assistant professor, department of obstetrics and gynecology, University of Pittsburgh, Magee-Women's Hospital, Magee Women's Research Institute.*

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Lung Health Experience



Charity Sunshine Tillemann-Dick performing at the CHEST Foundation Awards Ceremony.



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Breakfast of Champions



Young Professionals Reception



# Winners-All at CHEST 2016

We all know that, with the great success of CHEST 2016, 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 our annual meeting.

## CHEST Awards

College Medalist Award  
**Lewis J. Rubin, MD, FCCP**

Distinguished Service Award  
**Kim D. French, MHSA, CAPP, FCCP**

Alfred Soffer Award for Editorial Excellence  
**Seth J. Koenig, MD, FCCP**

Master Clinician Educator Award  
**Jack D. Buckley, MD, MPH, FCCP**

Distinguished Scientist Honor Lecture  
**Jay Nadel, MD**

Edward C. Rosenow III, MD, Master FCCP/  
Master Teacher Honor Lecture  
**Suhail Raoof, MBBS, FCCP**

Murray Kornfeld Memorial Founders Lecture  
**Michael Niederman, MD, FCCP**  
Pasquale Ciaglia Memorial Lecture  
**Kevin L. Kovitz, MD, FCCP**

Roger C. Bone Memorial Lecture  
**Robert A. Berg, MD**  
Thomas L. Petty, MD, Master FCCP  
Memorial Lecture  
**Nicola A. Hanania, MD, MS, FCCP**

Margaret Pfrommer Memorial Lecture in  
Long-term Mechanical Ventilation  
**Thomas G. Keens, MD**  
Om P. Sharma, MD, Master FCCP  
Memorial Lecture  
**Robert P. Baughman, MD, FCCP**

Early Career Educator  
**Gabriel Bosslet, MD, FCCP**

## CHEST Challenge Championship 2016

1st Place  
The University of Arizona  
**Huthayfa Ateeli, MBBS**  
**Naser Mahmoud, MD**  
**Muna Omar, MD, MBBS**  
PD: **James L. Knepler Jr.**

2nd Place  
New York Methodist Hospital  
**Anu R. Jacob, MD**  
**Stephen D. Milan, MD**  
**Jordan Taillon, MD**  
PD: **Anthony G. Saleh, MD, FCCP**

3rd Place  
Interfaith Medical Center  
**Chidozie C. Agu, MD**  
**Saroj P. Kandel, MBBS**  
**Divya Salhan, MD, MBBS**  
PD: **Marie Frances J. Schmidt, MD, FCCP**

## CHEST Foundation Grant Winners

GlaxoSmithKline Distinguished Scholar in  
Respiratory Health  
**Don Hayes Jr., MD, FCCP**  
The Research Institute at Nationwide  
Children's Hospital  
Implications of the Lung Allocation Score

in Prioritizing Critically Ill Patients for  
Lung Transplantation  
Supported by GlaxoSmithKline.

## 2016 Research Grantees

**Alice Turner, MBChB, MRCP, PhD**  
University of Birmingham, United  
Kingdom  
CHEST Foundation and the Alpha-1  
Foundation Research Grant in Alpha-1  
Antitrypsin Deficiency  
Improving Access to Augmentation: A  
Propensity-Matching Study Between the  
UK AATD Registry and AlphaNet  
This grant is jointly supported by the  
CHEST Foundation and the Alpha-1  
Foundation.

**Robert Busch, MD**  
Brigham and Women's Hospital,  
Channing Division of Network Medicine  
CHEST Foundation Research Grant in  
Chronic Obstructive Pulmonary Disease  
Methylation Quantitative Trait Loci:  
Markers of Race-Specific Disparities in  
African Americans With COPD  
This grant is supported by AstraZeneca.

**Clemens Grassberger, PhD**  
Massachusetts General Hospital –  
Harvard University  
CHEST Foundation Research Grant in  
Lung Cancer  
Dynamic FLT-PET as Biomarker for Early  
Response in Locally Advanced Lung  
Cancer Patients  
This grant is supported by Genentech Inc.

**Cristina Russo, MD, PhD**  
Bambino Gesù Children's Hospital, Rome,  
Italy  
CHEST Foundation Research Grant in  
Nontuberculous Mycobacteria  
A Proteomic-Metaproteomic Analysis  
Approach Allows Identification of  
Drug Target Candidates for the Future  
Design of Preventive, Diagnostic,  
and Therapeutic Strategies Against  
Nontuberculous Mycobacteria Diseases  
This grant is supported by Insmed.

**Peter Leary, MD, MS**  
University of Washington  
CHEST Foundation Research Grant in  
Pulmonary Arterial Hypertension  
Expression Profiling in Pulmonary Arterial  
Hypertension  
This grant is supported by Actelion  
Pharmaceuticals, US, Inc.

**Brett Ley, MD**  
University of California, San Francisco  
CHEST Foundation Research Grant in  
Pulmonary Fibrosis  
Extracellular Circulation RNAs as  
Predictors of Disease Progression in  
Idiopathic Pulmonary Fibrosis

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**Sydney Montesi, MD**  
Massachusetts General Hospital  
CHEST Foundation Research Grant in  
Pulmonary Fibrosis  
Gadofosveset-Enhanced Lung MRI to  
Detect Idiopathic Pulmonary Fibrosis  
Disease Activity

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**Farbod Rahaghi, MD, PhD**  
Brigham and Women's Hospital  
CHEST Foundation Research Grant in  
Venous Thromboembolism  
CT Scan-Based Markers for Prediction of  
Outcomes in Acute Pulmonary Embolism  
This grant is supported by Daiichi  
Sankyo.

**Catherine Oberg, MD**  
Icahn School of Medicine at Mount Sinai  
CHEST Foundation Research Grant in  
Women's Lung Health  
Effects of Household Air Pollution on  
Airway Inflammation, Lung Function,  
and Respiratory Symptoms  
This grant is supported in full by the  
CHEST Foundation.

## 2016 Community Service Grantee

**Ethel Jane Carter, MD, FCCP**  
Warren Alpert School of Medicine at  
Brown University  
CHEST Foundation Community Service  
Grant Honoring D. Robert McCaffree,  
MD, Master FCCP  
East African Training Initiative (EATI) in  
Pulmonary Medicine

## 2016 NetWorks Challenge Travel Grantees

**Debarsee Banerjee, MS, MD**  
Women's Health NetWork  
**Drew Harris, MD**  
Occupational and Environmental Health  
NetWork

**Kerry Hena, MD**  
Occupational and Environmental Health  
NetWork

**Amanpreet Kaur, MD**  
Women's Health NetWork

## 2016 Diversity Travel Grant Winners

**John B. Bishara, DO**  
**Renato F. Blanco Jr., MD**  
**Angel Coz-Yataco, MD**  
**Sherie A. Gause, MD**  
**Anthony Nebor, MD**  
**James T. Williams, MD**

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### Alfred Soffer Research Award Winners

Kerry Hena, MD

Deepak Pradhan, MD, FCCP

### Young Investigator Award Winners

Elizabeth Becker: Clinical Characteristics of Sarcoidosis in World Trade Center (WTC) Exposed Fire Department of the City of New York (FDNY) Firefighters

Daniel Altman, MD: Cost-Effectiveness of Universally Funding Smoking Cessation Pharmacotherapy

### Top 3 Poster Winners

Epaminondas Kosmas, MD, PhD, FCCP: Bronchiectasis in Patients With COPD: An Irrelevant Imaging Finding or a Clinically Important Phenotype?

Mark Regala, MD, BS: Evaluation of Outcomes of Post-Extubation Dysphagia in Elderly Patients

Massa Zantah, MD: Correlation of Esophageal Dilatation and Pulmonary Fibrosis in Scleroderma

Runner-up: Alev Gurgun, MD: Pulmonary Rehabilitation Response in Elderly and Younger Patients With COPD

### Case Report Slide Winners

John Egan, MD, BA: An Unusual Cause of Tracheal Stenosis Due to a Vascular Anomaly Successfully Managed With Silicone Airway Stenting Prior to Definitive Vascular Repair

Harpnett Grewal, MD: Bladder PTLT: First Reported Case of Post-Transplant Lymphoproliferative Disorder (PTLD) in the Bladder in a Lung Transplant Recipient

Michael Fingerhood, MD, MPH: Pulmonary Overlap Histiocytosis: A Rare Case of Interstitial Lung Disease Due to

Erdheim Chester Disease in a Patient With Langerhans Cell Histiocytosis and Myelodysplastic Syndrome

Yihenew Negatu, MD: Acute ST Elevation Myocardial Infarction Related to Carbon Monoxide Poisoning in a Young Patient Without Coronary Artery Disease

Stephanie Wappel, MD: False-Negative PET Imaging in Early Stage Malignant Pleural Mesothelioma

Lina Miyakawa, MD: Restrictive EGFR Mutation

Jeffrey Bonenfant, DO: A Unique Case of Follicular Bronchiolitis

Melissa Myers, MD: Seeing the Forest and Not Just the Trees: A Case of Recurrent Fever, Cough, and Respiratory Failure

Carly Fabrizio, DO: An Unusual Case of Submassive Hemoptysis

Meilinh Thi, DO: A Case to Make Your Skin Crawl

Garrett Harp, MD: Lambertosis: A Lung Cancer Mimic

Malik Khan, MD: Pleural Epithelioid Hemangioendothelioma: A Case Report

Priya Patel, MD: A Troubling Trifecta: Pulmonary Alveolar Proteinosis and Pneumocystis Pneumonia in Acute Myeloid Leukemia

Atul Palkar, MD: SGLT2 Inhibitors: Mind the Gap

Ji Yeon Lee, MD: Making Unusual Connections: Fibrosing Mediastinitis Leading to Bronchoesophageal Fistula

Sailm Daouk, MD: A Rare Form of Invasive Aspergillus Infection in a Severely Immunocompromised Host

Venkata Ravi Kumar Angirekula, MD: Vanishing Lung

Stephen Milan, MD: An Unexpected Mass

Lelia Logue, MD: A Rare Cause of Dysphagia

Daniel Hersherberger, MD: Rapidly Progressive Hypoxic Respiratory Failure After a Rash: A Case of Clinically Amyopathic Dermatomyositis (CADM)-Associated ILD

### Fellow Case Report Poster Winners

Krishna Siva Sai Kakkera

An Unusual Case of Cryptococcal Pleural Effusion

George Cheng

Use of Laparoscopic Suction Irrigator With Rigid Pleuroscope in Medical Thoracoscopy

Matt Koroscil

Wong Type Dermatomyositis Complicated by Interstitial Lung Disease

Derek Hansen

Acute Fibrinous and Organizing Pneumonia Following Hematopoietic Stem Cell Transplantation Responsive to Corticosteroid Therapy

Ala Eddin Sagar

Pulmonary Embolism Caused by Thrombin-Based Hemostatic Matrix After Discectomy

Sandeep Chennadi

Systemic Lupus Erythematosus (SLE) With Refractory Bilateral Chylothorax and Chylous Ascites

### Medical Student/Resident Case Report Poster Winners

Justin Fiala

Pulmonary Presentation Without Concurrent Bone Involvement in Erdheim-Chester Disease: A Report of Two Cases

Navitha Ramesh

A Fatal Migration: A Case of Intra-Cardiac Embolization of a Peripheral Stent

Humna Abid Memon

Use of Extracorporeal Membrane Oxygenation in Postpartum Management of a Patient With PAH

Vanessa Ohleyer

A Case of Unusual Anatomy for an Uncommon Mediastinal Tumor

Tanushree Gahlot

Three Unusual Presentations of Job's Syndrome (Hyper Immunoglobulin E Syndrome)

### NetWorks Challenge Winners

Round 1

Women's Lung Health NetWork

Round 2

Practice and Operations NetWork-1st place

Home-Based Mechanical Ventilation and Neuromuscular Disease NetWorks — 2nd place

Round 3

Home-Based Mechanical Ventilation, Neuromuscular Disease, and the Women's Lung Health NetWorks

### CHEST Bingo Winners

Youseff Anid, MD, FCCP

Karen Cochran, ACNP

Molly Howsware, DO

Katie Jeans, MD

Genovena Medina, RN

Gregory Eisinger, MD

Saurabh Mittal, MD, MBBS

Navitha Ramesh, MD

Dalvinder Dhillon, MD

Teresita Saylor, MD, FCCP

Carl Kaplan, MD, FCCP

Vishal Patel, MBBS, FCCP

Erin Peterson, CNP

Lilian Pereira, DO



Four women have served as CHEST Presidents, and three of them were able to catch up at CHEST in Los Angeles. From the left are Susan Pingleton, MD, Master FCCP; Barbara Phillips, MD, MSPH, FCCP; and Kalpalatha Guntupalli, MD, Master FCCP. Deborah Shure, MD, Master FCCP, our first woman President, is not pictured.



The CHEST Council of Global Governors met at CHEST in Los Angeles.

# NETWORKS: Pneumonia Day, evaluating inhalers, tobacco taxes

## Chest Infections

### Pneumonia Day: Today is the day to act!

This past November 12, we celebrated "Pneumonia Day," named for a disease that has little connotation in



DR. RESTREPO

the real world, because of the perception that we need only a short course of antibiotics to get better. Such is the origin of the term "walking pneumonia," which emphasizes that we can

still walk even while sick with pneumonia.

However, we recently experienced the most important moment of awareness related to this condition, when one of the U.S. presidential candidates became sick with that disease known as "pneumonia."

Suddenly, the media devoted great interest to explore this condition, as if it were a new outbreak or a rare disease that could potentially kill someone. Even the health-care providers seem to believe that "pneumonia" is not a big deal, ignoring the fact that it is the most common infectious cause of death overall, and that it not only affects children but also the elderly and patients with poor immune systems.

One out of nine patients who are admitted to the hospital for pneumonia may die during the hospitalization, and one out of four patients who get admitted to an ICU may not survive the event.

However, it also highlights that pneumonia is more than just an acute disease, compromising the brain, heart, and kidneys. In the long run, even after surviving the hospitalization for pneumonia, it can kill and cause other well-known complications leading to death, such as myocardial infarction, arrhythmias, heart failure, and sudden cardiac death.

Please, stop for one moment and ask yourself about your role in preventing pneumonia and pneumonia-related deaths in your communities. The Chest Infections NetWork is here to help you advocate for the common goal of solving this problem.

Marcos I. Restrepo, MD, MSc, FCCP  
Steering Committee Member

## Clinical Pulmonary Medicine

### Delivery makes a difference: Providing inhaled medication to your patients

One might ask why CHEST (Amer-

ican College of Chest Physicians) and Sunovion developed a steering committee of experts in the field of obstructive lung disease to evaluate the knowledge, attitudes, beliefs, and practices of physicians and other

health-care professionals related to inhalational medicines and devices. While inhalers are approved by the FDA Center for Drug Evaluation Research (CEDER) as drug and device

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combination, the process assesses reproducibility and shelf-life but does not address the real-world situation that each of us face with individual patients. How often do clinicians consider the characteristics of each delivery system, as well as the medication being delivered? One might be surprised at the answer.

Patients are frequently prescribed several types of devices with different instructions for optimal use. For example, dry powder inhalers often require high flow rates (30-90 L/min) to deaggregate powder pellets into particles less than 5  $\mu\text{m}$ , while metered-dose inhalers require a slow inspiratory flow (less than 30 L/min). Patients who use both types of devices often confuse which

inspiratory flow rate to use with which devices, despite proper education and training. This does not even take into consideration the variable number of steps required by various inhalational devices (which can be as few as 3 steps to as many as 12 steps). Additionally, studies demonstrate that peak inspiratory flow rates, inspiratory volumes, and drug deposition in the lungs may be



DR. PETERS

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influenced by gender, height, and weight; as well as by the degree of pulmonary reserve and hyperinflation.

Are there data to suggest that these questions impact the care of patients with severe asthma or COPD? I eagerly await the results of the survey.

*Jay I. Peters, MD, FCCP  
Steering Committee Member*

## Interprofessional Team

### A California victory for tobacco control

Californians approved Proposition 56, "Cigarette Tax to Fund Healthcare, Tobacco Use Prevention, Research, and Law Enforcement." This measure increases the excise tax on all forms of tobacco by \$2.00. For the first time, it applies to electronic prod-

ucts that vaporize nicotine that were previously only subject to sales tax. This is in addition to federal excise taxes (\$1.01) and state and local sales taxes (\$0.50 to \$0.60). ([https://ballotpedia.org/California\\_Proposition\\_56,\\_Tobacco\\_Tax\\_Increase\\_\(2016\)](https://ballotpedia.org/California_Proposition_56,_Tobacco_Tax_Increase_(2016)))

When Prop 56 goes into effect April 1, 2017, the average price of a package of cig-

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DR. ROTH

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arettes will increase to at least \$7.89. Based on data from the Surgeon General's report on "Preventing Tobacco Use Among Youth and Young Adults," this tax increase should equate with a fall in smoking rates by about 12%. Youth and young adults

are particularly susceptible to price increases, which helps prevent smoking initiation or continuation.

Tobacco-related health-care costs Californians \$3.5 billion dollars annually (Official Voter Information Guide, 2016). Funds raised by Prop 56 will be used by state and local health programs such as Medi-Cal to

defray the costs of smoking prevention programs, smoking cessation, and treatment of tobacco-related illnesses (California Tobacco Control Program).

Prop 56 expands on tougher laws implemented in 2016 that expanded the workplace prohibition of smoking, increased fees for tobacco

retailers and wholesalers, broadened the definition of smoking to include e-cigarettes, and increased the minimum age to purchase tobacco to 21 years old. Combined, these measures are expected to result in a further decline in tobacco usage in California.

*Alan Roth, RRT, MS, FCCP  
Steering Committee Member*

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# Bronchoscopy sedation changes in 2017

BY MICHAEL NELSON, MD, FCCP

A major change in coding for bronchoscopy occurred on January 1, 2017, as moderate (conscious) sedation is now separately identified

from the work relative value units (wRVUs) for the bronchoscopy codes. While traditionally the bronchoscopist provided moderate sedation, in recent clinical practice, other individuals often provide the sedation. CMS mandated

refinement of separate Current Procedural Terminology (CPT®) codes to account for the work of moderate procedural sedation. In the final rule published in November 2016, CMS removed 0.25 wRVUs from many of

the bronchoscopy codes to account for the work of moderate sedation. To be reimbursed appropriately, include a moderate sedation CPT code with all bronchoscopy procedures.

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Total intraservice time	Patient age	Moderate sedation performed by	
		Bronchoscopist	Second provider
		Codes	Codes
Less than 10 minutes	Any age	Not reported separately	
15-22 minutes	< 5 years	99151	99155
	>5 years	99152	99156
23-37 minutes	< 5 years	99151 + 99153	99155 + 99157
	>5 years	99152 + 99153	99156 + 99157
38-52 minutes	< 5 years	99151 + 99153 x2	99155 + 99157 x2
	>5 years	99152 + 99153 x2	99156 + 99157 x2

Continued from previous page

Use codes **99151** and **99155** for patients younger than 5 years. For a patient 5 years or older, when the bronchoscopist provides moderate sedation, report code **99152** for the initial 15 minutes and **99153** for subsequent time in 15-minute increments. For a patient

5 years or older, when a provider other than the bronchoscopist provides moderate sedation, use code **99156** for the initial 15 minutes and **99157** for subsequent time in 15-minute increments. Utilize codes **99156** and **99157** only when a second provider (other than the bronchoscopist) performs moderate sedation in the facility setting (eg, hospital, outpatient hospital/ambulatory surgery center, skilled nursing facility). When the second provider performs these services in the nonfacility setting (eg, physician office, freestanding imaging center), do not report codes **99155**, **99156**, or **99157**. Moderate sedation does not include minimal sedation (anxiolysis), deep sedation, or monitored anesthesia care (**00100-01999**).

Do not use a moderate sedation code (**99151-2** or **99155-6**) if providing less than 10 minutes of moderate sedation. As with other time-based codes, use the subsequent codes **99153** and **99157** when moderate sedation lasts 8 minutes or longer than the initial 15 minutes. The time for moderate sedation begins with the administration of the sedating agent and concludes when the continuous face-to-face presence of the bronchoscopist ends after completion of the procedure. Intermittent, re-evaluation of the patient afterward is postservice work and is not included in the time for moderate sedation. For example, if the bronchoscopist provides moderate sedation for 25 minutes in a 65-year-old man, report **99152** (for the initial 15 minutes) and **99153** (for the subsequent 10 minutes). If an individual other than the bronchoscopist provides moderate sedation for 41 minutes in a 57-year-old woman, use **99156** (for the initial 15 minutes) and two units of **99157** (for the subsequent 26 minutes). If a bronchoscopist provides moderate sedation and reports the appropriate codes after January 1, the 0.25 wRVU change will have no financial impact compared with 2016. If a second provider performs the moderate sedation, expect an approximately \$8.72 drop in reimbursement per procedure.

IMPORTANT REMINDER

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The deadline for claiming CME/MOC for CHEST 2016 is February 28, 2017. Additionally, due to a deadline imposed by ABIM, all MOC from all 2016 activities must be claimed by February 28, 2017. After this date, ABIM will no longer accept MOC from 2016 activities. Please note: depending on your recertification cycle, you may need points prior to the 2017 deadline. Please refer to your ABIM diplomate’s record and/or contact ABIM for questions specific to your individual board certification.

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Join leaders in CHEST medicine for a program designed by clinicians for clinicians.

The Joint Congress organized by CHEST and the Swiss Society of Pneumology will be held from June 7-9 in Basel, Switzerland. The program has been designed by more than 140 faculty members from both the United States and Europe, and it aims to provide a robust overview of all aspects of respiratory medicine through interactive sessions, plenary discussions, critical appraisals on controversial topics, and a review of the last year of published works.

The Joint Congress also provides the opportunity to take part in hands-on simulation in areas such as lung function techniques including body plethysmography, N<sub>2</sub> washout techniques, and respiratory physiotherapy. Another hands-on opportunity is the interventional pneumology CHEST experience

course, which will be held from 8:00 AM-11:00 AM on June 7 and 8 on site. This course will provide an overview of conventional and EBUS-guided TBNA, an anatomy identification of airway nodes, management of airway bleeding, and management of pneumothorax. This course is ideal for clinicians and health-care professionals with specialties in pulmonary, critical care, and intensive care medicine, as well as thoracic surgery.

The program at the Joint CHEST-SGP Congress aims to improve the patient care abilities of every attendee, as well as provide an ideal environment for networking with leaders in your field.

The call for abstracts remains open until January 24, 2017. The abstract topic areas are:

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- Sleep/Breathing
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- Pulmonary hypertension
- Basic science
- Thoracic surgery
- Pediatrics

All abstracts must be submitted via the Joint Congress abstracts web portal [www.chest-sgp-switzerland2017.org](http://www.chest-sgp-switzerland2017.org).

CHEST recognizes the value of international outreach, and this Joint Congress advances that initiative. CHEST aims to standardize the patient care across borders and to encourage international collaboration to build the

future of chest medicine. To further this mission, an application has been made to the European Accreditation Council for Continuing Medical Education (EACCME®) for CME accreditation of this event. Additionally, an application has been made to the European Board for Accreditation in Pneumology (EBAP) to provide quality assurance and CME for the event.

For more information or to register, visit the CHEST Joint Congress website [www.chest-sgp-switzerland2017.org](http://www.chest-sgp-switzerland2017.org). Early registration ends on March 16, 2017.



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## In Memoriam

*CHEST has been informed of the following members' deaths. We extend our sincere condolences.*

**Anthony Cosentino, MD, FCCP**  
(January 2016)

**Ben Branscomb, MD** (July 2016)

**Steven Sahn, MD, FCCP** (Aug 2016)

**Thomas Aldrich, MD** (September 2016)

**John C. Baldwin, MD, FCCP**  
(September 2016)

**David Cugell, MD, FCCP**  
(December 2016)



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#### Cardiopulmonary Exercise Testing

September 22-24

#### Critical Care Ultrasound: Integration into Clinical Practice

November 10-12

# Adding respiratory rate to triage criteria improves accurate staging of chest trauma patients

BY MICHELE G. SULLIVAN  
Frontline Medical News

WASHINGTON – Adding respiratory rate and suspected blunt chest injury to a trauma assessment in the field significantly improved the appropriate triaging of level III trauma patients.

When the assessment specifically evaluated for tachypnea in the setting of blunt chest injury, undertriaging improved by 1.2%, John Yonge, MD, said at the annual clinical congress of the American College of Surgeons.

“When we applied this new criteria to our 10-year study, we identified 661 patients who should have been activated as a level I or level II,” but instead were assessed as less critically injured, Dr. Yonge said in an interview. This initial misstep significantly extended the time before patients could have critical surgical procedures and was related to higher mortality among them.

Dr. Yonge, a surgical fellow at Oregon Health & Science University, Portland, and his mentor Martin Schreiber, MD, conducted the retrospective study of 7,880 trauma patients admitted at level III activation from 2004 to 2014. The OHSU trauma system has three activation levels.

- Level I activations are reserved for the most critically injured patients; attending trauma surgeon and anesthesiologist presence is mandatory.
- Level II activations capture moderate to severe injuries; trauma surgeon and respiratory therapist presence is mandated.

- Level III activations are designed to capture patients who do not require an immediate lifesaving intervention; the presence of the trauma surgery chief resident and attending emergency medicine physician is mandatory.



DR. YONGE

Patients were considered undertriaged if they were admitted as level III activations, but then required a critical intervention (chest tube placement, intubation, needle thoracostomy, or intracranial pressure monitoring) in the emergency department or ultimately met level I or II activation criteria.

Among all the level III patients, 466 (6%) were undertriaged: 390 were undertriaged based on the existing level I or II activation criteria, and 76 were considered undertriaged based on the need for a critical intervention.

Most of the undertriaged patients (65%) met criteria for level I activation; the rest should have been triaged as level II patients. Compared with appropriately staged level III patients, mortality among the undertriaged patients was significantly higher (3.2% vs. 0.6%). Undertriaged patients also experienced longer delays before initiation of major emergency surgery: a mean of 147 minutes,

compared with 106 minutes for appropriately triaged level I patients and 62 minutes for appropriately triaged level II patients.

Dr. Yonge then looked for clinical measures that would improve triage. Tachypnea (respiratory rate of more than 20 breaths per minute) in the field stood out as a significant factor. Tachypneic patients who had a suspected chest injury were 70% more likely to be undertriaged than were those with a normal respiratory rate. Tachypnea was significantly associated with a diagnosis of flail chest, emergency department intubation, and chest tube placement.

The team then constructed a new triage criterion for patients with suspected chest injury – tachypnea combined with suspected blunt thoracic injury. By applying that model to their study population of level III patients, they determined that the level III undertriage rate would be reduced by 1.2%.

Tying the physiologic marker of tachypnea to a suspected clinical diagnosis is a key factor, Dr. Yonge noted. “Just adding tachypnea doesn’t help us. In fact, it would overwhelm us, because a trauma patient could very well be tachypneic because he’s experiencing panic. But tying it to a suspected clinical diagnosis gives us a meaningful result.”

He confirmed this linkage with an additional analysis. “We looked to see how severely injured these patients were and found that 71% of them had an Abbreviated Injury Score (AIS) to

the chest of 3 or more, indicating a severe chest injury. Only 29% had an AIS of 2 or less. So this proves that respiratory rate is a valid triage criterion and can be used to identify patients who need a higher level of trauma care.”

The challenge now, Dr. Yonge said, is incorporating the marker into clinical practice. “It doesn’t matter how many statistics you do, if you can’t

**Tying the physiologic marker of tachypnea to a suspected clinical diagnosis is a key factor, Dr. Yonge noted.**

**“Just adding tachypnea doesn’t help us. In fact, it would overwhelm us ...”**

educate the prehospital providers in this, it’s useless. They are the crux of the trauma system.”

Although national guidelines do recommend assessing respiratory rate as part of field triage, it often isn’t recorded or is only estimated, Dr. Yonge said. That’s one reason he used the 20-breaths-per-minute cutoff rate. “It doesn’t even take a full minute to assess this, but it can make a big improvement in care.”

Neither he nor Dr. Schreiber had any financial disclosures.

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## Confirmatory CT prevents unnecessary bronchoscopy

BY M. ALEXANDER OTTO  
Frontline Medical News

It’s probably a good idea to do a repeat CT the morning of a scheduled bronchoscopy to make sure the pulmonary nodule is still there, according to investigators from Johns Hopkins University, Baltimore.

From Jan. 2015 to June 2016, 116 patients there were scheduled for navigational bronchoscopy to diagnose pulmonary lesions found on screening CTs. Eight (6.9%) – four men, four women, with an average age of 50 years – had a decrease in size or resolution of their lesion on confirmatory CT, leading to cancellations of their procedure. The number needed to screen to prevent one unnecessary procedure was 15. For canceled cases, the average time from screening CT to scheduled bronchoscopy was 53 days; for patients who underwent a bronchoscopy, it was 50 days (Ann Am

Thorac Soc. 2016 Dec;13[12]:2223-8).

It can take months to schedule a bronchoscopy after a pulmonary nodule is found on CT screening. Once in a while, the investigators and others have found, even suspicious nodules resolve on their own, and patients end up having a bronchoscopy they don’t need.

“If there is a significant delay from the initial imaging, practitioners should consider repeat studies before proceeding with the scheduled procedure ... Same-day imaging may decrease unnecessary procedural risk ... The optimal time that should be allowed to pass is difficult to ascertain,” said investigators led by Roy Semaan, MD, of the division of pulmonary and critical care medicine at Hopkins.

The team used a newer version of electromagnetic navigation bronchoscopy (Veran Medical Technologies, St. Louis), which requires expiratory and inspiratory CTs the morning of the procedure so software can build a virtual airway model to lo-

calize the nodule.

In addition to nodule resolution, same-day CTs might identify disease progression that alters the diagnostic plan of care.

“The most obvious risk associated with repeat CT imaging is the increased radiation exposure to the patient. Patients in our study who received inspiratory and expiratory CT scans ... had a mean exposure of 9.485 mSv, which is not “negligible, but one-time doses at this range are generally considered to be low risk for contributing to the future development of a malignancy,” the team said.

The extra cost of a same-day noncontrast chest CT – about \$300, the authors said – is more than offset if it cancels “an unnecessary procedure with its associated risks,” they said.

Dr. Semaan had no disclosures. Three investigators reported grants and personal fees from Veran.

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# Recovery path complicated with post-trauma VTE

BY DOUG BRUNK  
Frontline Medical News

CORONADO, CALIF. – Patients who develop a venous thromboembolism (VTE) following severe hemorrhage are more susceptible to complications, compared with their counterparts who do not; they also exhibit hypercoagulability and enhanced platelet function at admission, and have delayed recovery of coagulation and platelet function following injury.

Those are the key findings from a secondary analysis of data from the Pragmatic Randomized Optimal Platelet and Plasma Ratio (PROPPR) trial, which randomized 680 severely injured trauma patients from 12 level I trauma centers to receive 1:1:1 or 1:1:2 ratios of plasma to platelets to red blood cells (JAMA 2015;313[5]:471-82). “The prevention of VTE following traumatic injury is an ongoing challenge,” Belinda H. McCully, PhD, said at the annual meeting of the Western Surgical Association. “Despite prophylaxis, about 25% of patients present with VTE, which is associated with higher complications and an increased

risk for mortality. Common risk factors for mortality include age, body mass index, extremity injury, and immobility, but the precise mechanisms that contribute to VTE development are not well understood. We do know that the three main factors contributing to thrombosis include static flow, endothelial injury, and hypercoagulability. Clinically, coagulation is the most feasible factor to assess, mainly through the use of conventional coagulation tests, thromboelastography, platelet levels, and platelet function assays.” However, she continued, severe hemorrhage can lead to a hypocoagulable state that is further exacerbated by hemodilution, acidosis, and hypothermia, creating traumatic-induced coagulopathy. “Despite this hypocoagulable state,



Preventing VTE after trauma is a challenge, noted Dr. McCully.

VTEs are still present in this patient population.”

Dr. McCully of the division of trauma, critical care, and acute care surgery in the department of surgery at Oregon Health & Science University, Portland, and her associates hypothesized that enhanced, earlier recovery of coagulation function is associated with increased VTE risk in severely injured trauma patients. To test this hypothesis, they conducted a secondary analysis of the PROPPR database, excluding patients who received anticoagulants, to rule out any bias against VTE development, as well as patients who died within 24 hours, to reduce the survival bias. This left 558 patients: 475 who did not develop a VTE, and 83 who did (defined as those who developed deep vein thrombosis or pulmonary embolism). Patient characteristics of interest included age, sex, BMI, mechanism of injury, and injury severity, as well as the transfusion group, the type of blood products given, and the percentage of patients given procoagulants. The investigators also assessed length of stay and complication incidence previously defined by the trial. During the trial, blood samples were taken from admission up to 72 hours and were used to assess both whole blood coagulation using thromboelastography and platelet function using the Multiplate assay.

Dr. McCully reported that VTE patients and non-VTE patients demonstrated similar admission platelet function activity and inhibition of

all platelet function parameters at 24 hours ( $P$  less than .05).

The onset of platelet function recovery was delayed in VTE patients, specifically for arachidonic acid, adenosine-5'-diphosphate, and collagen. Changes in thromboelastography, clot time to initiation, formation, rate of formation, and strength and index of platelet function from admission to 2 hours indicated increasing hypocoagulability ( $P$  less than .05) but suppressed clot lysis in both groups. Compared with patients in the non-VTE group, the VTE group had lower mortality (4% vs.

13%) but increased total hospital days (a mean of 30 vs. 16;  $P$  less than .05).

Adverse outcomes were also more prevalent in the VTE group, compared with the non-VTE group, and included systemic inflammatory response syndrome (82% vs. 72%), acute kidney injury (36% vs. 26%), infection (61% vs. 31%), sepsis (60% vs. 28%), and pneumonia (34% vs. 19%;  $P$  less than 0.05 for all associations). Conversely, regression analysis showed that VTE was associated only with total hospital days (odds ratio, 1.12), while adverse events were similar between the two groups. “From this we can conclude that VTE development following trauma may be attributed to hypercoagulable thromboelastography parameters and enhanced platelet function at admission, and compensatory mechanisms in response to a delayed recovery of coagulation and platelet function,” Dr. McCully said.

She acknowledged certain limitations of the study, including the fact that it was a secondary analysis of prospectively collected data. “We also plan to assess plasma markers of clot strength and fibrinolysis, which is an ongoing process,” she said. “Despite excluding patients that died within 24 hours, there was still a survival bias in the VTE group.”

The PROPPR study was supported by the National Heart, Lung, and Blood Institute and by the Department of Defense.

Dr. McCully reported having no relevant financial disclosures.

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# Steroids could reduce death rate for some TB patients

BY JENNIE SMITH  
Frontline Medical News

**T**uberculosis patients admitted to intensive care units with acute respiratory failure had significantly better survival at 90 days after treatment with corticosteroids and anti-TB drugs, compared with patients not treated with the steroids, according to a retrospective study.

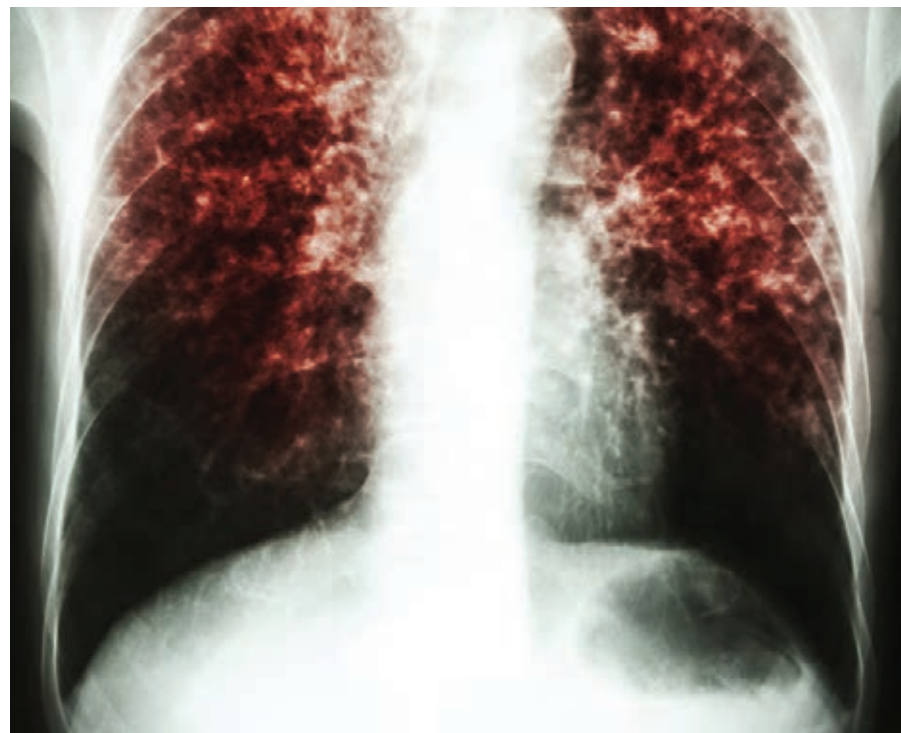
An adjusted inverse probability of treatment weighted analysis using propensity scores revealed corticosteroid use to be independently associated with a significantly reduced 90-day mortality rate (OR = 0.47; 95% CI, 0.22-0.98). This statistical approach was used because it reduces selection bias and other potential confounding factors in a way that a multivariate analysis cannot, wrote Ji Young Yang, MD, of Busan (South Korea) Paik Hospital and Inje University College of Medicine in Busan.

The study involved the examination of records of 124 patients (mean age 62, 64% men) admitted to a single center over a 25-year period ending in 2014. Of these, 56.5% received corticosteroids, and 49.2% of the cohort died within 90 days.

Mortality rates were similar between the steroid-treated and non-steroid-treated groups (48.6% and 50%, respectively), and unadjusted 90-day mortality risk was not affected by steroid administration (odds ratio, 0.94; 95% CI, 0.46-1.92;  $P = .875$ ), reported Dr. Yang and colleagues (Clin Infect Dis. 2016 Sep 8. doi: 10.1093/cid/ciw616).

The investigators acknowledged that their study was limited by various factors, including its small size, its use of data from a single center, and its lack of a standardized approach to steroid treatment.

“Further prospective randomized controlled trials will therefore be necessary to clarify the role of steroids in the management of these patients,” they wrote in their analysis. However, Dr. Yang and colleagues argued, in acute respiratory failure – a rare but dangerous complication in TB – “corticosteroids represent an attractive option because they can suppress cytokine expression and are effective in managing the inflammatory complications of extrapulmonary tuberculosis. Moreover, corticosteroids have been recently been shown to reduce mortality or treatment failure in patients with tuber-



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***Mycobacterium tuberculosis* infection (pulmonary tuberculosis)**

culosis or severe pneumonia.”

Robert C. Hyzy, MD, FCCP, director of the critical care medicine unit at the University of Michigan, Ann Arbor, said the findings “should be considered hypothesis generating.

“Clinicians should wait for prospec-

tive validation of this observation before considering the use of corticosteroids in hospitalized patients with tuberculosis,” he added.

Dr. Yang and colleagues disclosed no conflicts of interest or outside funding for their study.



#### Collaborators

This activity is presented through an educational collaboration by the American College of CHEST Physicians (CHEST), the American Society of Clinical Pathology, the National Comprehensive Cancer Network® (NCCN®), and The France Foundation.

This activity is supported by educational grants from Merck and AstraZeneca.

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# More restrictive hemoglobin threshold advised

BY BIANCA NOGRADY  
Frontline Medical News

New guidelines on red blood cell blood transfusion recommend a restrictive threshold in which transfusion is not indicated until the hemoglobin level is 7-8 g/dL for most patients, finding that it is safe in most clinical settings.

The updated clinical practice guidelines on transfusion thresholds and storage from the AABB (formerly known as the American Association of Blood Banks), also note that red blood cell units can be used at any time within their licensed dating period, rather than a preference being given to fresher units less than 10 days old.

The guidelines, published online Oct. 12 in JAMA, are an update of the 2012 transfusion guidelines, and are a response to a more than doubling of the number of patients since enrolled in randomized controlled trials of red blood cell transfusions.

The AABB's clinical transfusion medicine committee, led by Jeffrey L. Carson, MD, of Robert Wood Johnson Medical School, New Brunswick, N.J., analyzed data from 31 randomized controlled trials of 12,587 participants, which compared restrictive transfusion thresholds of 7-8 g/dL to more liberal thresholds of 9-10 g/dL.

This analysis showed that the use of restrictive transfusion protocols was associated with an absolute difference in 30-day mortality of three fewer deaths compared to the more liberal thresholds. There was no significant difference in 30-day mortality in trials that compared a threshold of 8-9 g/dL to a threshold of less than 7 g/dL (JAMA 2016, Oct 12. doi: 10.1001/jama.2016.9185).

"For all other outcomes evaluated, there was no evidence to suggest that patients were harmed

by restrictive transfusion protocols, although the quality of the evidence was low for the outcomes of congestive heart failure and rebleeding," the authors reported.

Based on these findings, they recommended a restrictive red blood cell transfusion threshold, in which transfusion is not indicated until the hemoglobin level is 7 g/dL for hospitalized adult patients who are hemodynamically stable, including critically ill patients.

However for patients undergoing orthopedic or cardiac surgery, or those with preexisting cardiovascular disease, they advised a threshold of 8 g/dL for initiating a red blood cell transfusion.

They also stressed that these recommendations did not apply to patients with acute coronary syndrome, those with severe thrombocytopenia, those treated for hematologic or oncologic disorders who at risk of bleeding, and those with chronic transfusion-dependent anemia, citing a lack of quality randomized controlled trial evidence.

The guideline authors examined the issue of the optimal length of time that red blood cell units should be stored, pointing out that there is currently no formal guidance on the optimal period of red blood cell storage prior to transfusion.

While units of red blood cells can be stored for up to 42 days, the committee said there was some evidence that longer storage may be associated with adverse transfusion outcomes.

"The RBCs stored for longer periods have decreased ability to deliver oxygen due to decreased levels of 2,3-diphosphoglycerate, decreased nitric oxide metabolism, alterations of the RBC membrane leading to increased rigidity, and increased RBC endothelial adherence," they wrote.

Despite this, the review of 13 randomized controlled trials examining the effect of storage dura-

## VIEW ON THE NEWS

### Nirmal S. Sharma, MD, FCCP, comments:

These recommendations are very helpful and are now part of standard ICU care in several centers. Our experience in clinical practice has shown that even patients supported with extracorporeal membrane oxygenation (ECMO) for acute lung failure or as a bridge to lung transplantation on VV ECMO can safely tolerate a lower transfusion threshold (7-8g/dL.) Future well-designed trials are needed to advocate its safety in patients supported with extracorporeal life support technologies.



tion found no evidence that fresher units had any impact on mortality compared to standard issue units, nor were there any more adverse events with the standard issue units.

The absolute difference in 30-day mortality was four more deaths per 1,000 with fresher blood, and there was a higher risk of nosocomial infections among patients who received fresher red blood cell units although the authors said the quality of evidence was low.

They therefore recommended that no preference be given to fresher red blood cell units, and that all patients be treated with units chosen at any point within their licensed dating period.

Guideline development was supported by AABB. Four authors declared grants, fees, stock options or consultancies from pharmaceutical companies, but no other conflicts of interest were declared.

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## Macrolide monotherapy works in some NTM lung disease

*Most with NTM lung disease plus Mycobacterium massiliense were successfully treated*

BY JENNIE SMITH  
Frontline Medical News

FROM CHEST

Patients with cystic fibrosis or bronchiectasis and one form of *Mycobacterium abscessus* disease can be successfully treated with long-term oral macrolide monotherapy following short-term intravenous combination antibiotic therapy, a Korean research team has shown.

The *M. abscessus* complex is implicated in between a fifth and half of all cases of lung disease caused by nontuberculous mycobacteria (NTM). Though treatment is notoriously dif-

ficult and prolonged in all NTM lung disease, one subspecies of *M. abscessus* – *M. massiliense* – lacks the active gene needed for developing resistance to macrolide-based antibiotics, making it potentially more readily treated.

In research published in CHEST, Won-Jung Koh, MD, of Samsung Medical Center and Sungkyunkwan University in Seoul, South Korea, and colleagues, sought to determine the optimal treatment protocol for patients with massiliense disease (Chest. 2016 Dec;150[6]:1211-21). They identified 71 patients with massiliense disease who had initiated antibiotic treatment between January 2007 and

December 2012. These patients were part of an ongoing prospective cohort study on NTM lung disease. The first 28 patients in the study were hospitalized for 4 weeks and treated with intravenous amikacin and cefoxitin along with oral clarithromycin and a fluoroquinolone. Following discharge, these patients remained on the oral agents for 24 months.

Two years into the study, the protocol changed, and the next 43 patients were treated with a 2-week course of intravenous amikacin and cefoxitin along with the oral agents. In some patients, azithromycin, which came into use in Korea for NTM lung disease in 2011, replaced a fluoroquinolone. After discharge, all patients stayed on the oral mac-

*Continued on following page*



Continued from previous page

rolides (with seven also taking a fluoroquinolone) until their sputum cultures were negative for 12 months.

For the patients treated for 4

weeks, the response rates after 12 months of treatment were 89% for symptoms, 79% for computed tomography, and 100% for negative sputum cultures. In the patients treated for 2 weeks, they were 100%, 91%,

and 91%, respectively. None of these differences between the two groups were statistically significant. Median total treatment duration, however, was significantly shorter – by nearly a year – in the 2-week plus macrolide monotherapy group than in the other group of patients (15.2 months vs. 23.9 months,  $P$  less than .001).

Acquired macrolide resistance developed in two patients in the group who received a 2-week course of intravenous amikacin and cefoxitin along with the oral agents, including one case of high-level clarithromycin resistance. Genotyping revealed reinfection with different strains of *M. massiliense*.

“[Oral] macrolide therapy after an initial 2-week course of combination antibiotics, rather than long-term

parenteral antibiotics, might be effective in most patients with *M. massiliense* lung disease,” Dr. Koh and colleagues wrote, noting that multicenter randomized trials would be needed “to assess the efficacy” of the findings.

The Korean government funded Dr. Koh and colleagues’ study. None of the authors disclosed conflicts of interest.

## VIEW ON THE NEWS

### “Risk/benefit balance” does not favor macrolide monotherapy use

“In this study by Koh et al., it is gratifying that most patients had a favorable microbiologic outcome. It is also somewhat surprising that only two patients developed acquired macrolide resistant *M. abscessus* subsp *massiliense* isolates. While the absolute number is low, for those two individuals, the consequences of developing macrolide resistance are far from trivial. They have transitioned from having a mycobacterial infection that is relatively easy to treat effectively to a mycobacterial infection that is not,” David E. Griffith, MD, FCCP, and Timothy R. Aksamit, MD, FCCP, wrote in an editorial published in the December issue of CHEST (Chest. 2016 Dec;150[6]:1177-8).

The authors noted that they “enthusiastically applaud and acknowledge the prolific and consistently excellent work done by the group in South Korea, but we cannot endorse the widespread adoption of macrolide monotherapy for” this patient group. “In our view, the risk/benefit balance of this approach does not favor macrolide monotherapy even though the majority of patients in this study were adequately treated.”

*Dr. Griffith is professor of medicine at University of Texas Health Science Center, Tyler, and Dr. Aksamit is a consultant on pulmonary disease and critical care medicine at the Mayo Clinic, Rochester, Minn. They disclosed no conflicts of interest.*

## CORRECTION

On page 7 of the November issue of CHEST Physician, the third sentence of the fourth paragraph contained an error. The sentence should have read, “They were randomized to infusions of reslizumab 3.0 mg/kg or placebo given once every 4 weeks for 16 weeks.”

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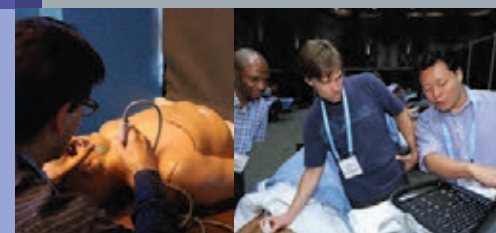
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# Blood assay rapidly identifies lung cancer mutations

BY M. ALEXANDER OTTO  
Frontline Medical News

AT CHEST 2016

LOS ANGELES – A newer blood test (GeneStrat from Biodesix) identified genetic mutations in lung tumors in about 24 hours, allowing for an early start of mutation-specific chemotherapy, in an investigation from Gundersen Health System in La Crosse, Wis.

Researchers drew blood samples when they performed biopsies on 84 patients with highly suspicious lung nodules and submitted both blood and tissue for mutation analysis. The blood was analyzed by Biodesix, the maker of GeneStrat, a commercially available digital droplet polymerase chain reaction assay launched in 2015. The company sent the results back in an average of 24.1 hours, and all within 72 hours.

The mutation results from tissue analysis took 2-3 weeks.

Fifteen patients (18%) had epidermal growth factor receptor (EGFR) mutation, echinoderm microtubule-associated-protein-like 4 and anaplastic lymphoma kinase (EML4-ALK) gene fusion, or K-Ras protein gene mutation. Those with EGFR or EML4-ALK mutations were candidates for targeted therapy. Compared with tissue testing, the blood assay had a sensitivity of 88% and a specificity of 99%. The tissue testing picked up two mutations missed by blood testing. One of the two mutations is rare and was not included in the blood assay. Meanwhile, the assay caught a mutation missed on tissue analysis.

"I was surprised" by the results. "I didn't expect to have that level of concordance [96%] between



DR. MATTINGLEY

blood and tissue. I thought we would miss a lot more with blood," but tissue and blood testing were "nearly equivalent," said lead researcher and interventional pulmonologist Jennifer Mattingley, MD, at the annual meeting of the American College of Chest Physicians.

She and her colleagues are now routinely using GeneStrat to guide initial lung cancer therapy. "[The turnaround time] allows us to have [the mutation status] when oncologists meet with patients for the very first time," she said.

It "definitely" makes a difference. "If you have an actionable mutation and there's a targeted chemothera-

py" – such as erlotinib (Tarceva) for epidermal growth factor receptor mutation patients – it can be started right out of the gate. "Time to treatment is very important," not just psychologically for patients but also for them to have the best chance against the tumor. The sooner "we can start a targeted therapy," the better outcomes are likely to be, Dr. Mattingley said.

When mutation status is delayed, patients might be started "on the wrong therapy upfront, and it's really hard to back up and start over again," she said.

"Once we give patients a diagnosis of lung cancer, the next thing they should hear right away is how we are going to attack it. We felt strongly [that there was a] need to look at this to see if we could truly expedite the time from diagnosis to treatment. We

*Continued on following page*

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# Half of MPE patients received unneeded treatment

BY M. ALEXANDER OTTO  
Frontline Medical News

AT CHEST 2016

LOS ANGELES – About half of patients with symptomatic malignant pleural effusions at McGill University Health Centre in Montreal had unnecessary procedures and hospital admissions before definitive treatment with chemical pleurodesis or indwelling pleural catheters, according to researchers.

Instead of chest taps to relieve symptoms followed by referrals for definitive treatment, some patients got chest tubes – without pleurodesis – after presenting to the emergency department and being referred to radiology; they were then admitted to the hospital for a few days while the tubes were in place. In short, cancer patients were wasting what time they had left on medical care they didn't need, and incurring unnecessary costs, said lead investigator Benjamin Shieh, MD, formerly at McGill but now an interventional pulmonology

fellow at the University of Calgary.

McGill is a tertiary care center able to perform both definitive procedures, so “we should be a center of excellence. I imagine there are similar situations” at other hospitals, especially those without the resources of McGill, Dr. Shieh said at the annual meeting of the American College of Chest Physicians.

McGill has taken several steps to address the problem, including early ED referral to the pulmonology service and discouraging radiology from placing chest tubes for malignant pleural effusions (MPE). “I think we can avoid a big proportion of hospitalizations for MPE, and certainly a proportion of repeat [ED] visits,” said senior author Anne Gonzalez, MD, an attending pulmonologist at McGill.

The investigators looked into the issue after noting that a significant number of patients with MPE had been hospitalized with chest tubes. They reviewed 72 symptomatic MPE cases in 69 patients treated in 2014 and 2015. The patients were 70 years



DR. SHIEH



DR. GONZALEZ

old, on average, and about 60% were women. Lung and breast were the most common cancers.

Management was ideal in 36 cases (50%), meaning that, prior to definitive treatment, patients had no more than two pleural taps for symptom relief, no more than one ED visit, no chest tubes without pleurodesis, and no hospitalizations. “We thought this would be reasonable to try to achieve for MPE,” since there's no definition of ideal management, Dr. Shieh said.

Nonideal patients had a mean of 2.5 pleural procedures – almost twice the number in the ideal group – before definitive palliation, with no respiratory

consult beforehand. Chest tubes were placed in 27 cases (38%) for an average of 3.7 days; 28 patients (39%) were hospitalized. Nonideal patients were far more likely to present first to the ED, and ED presentations were more likely to get chest tubes and be admitted. All the cases were eventually treated definitively, 68 with indwelling pleural catheters and 4 by thorascopic talc insufflation. Time from initial presentation to definitive palliation was about 1 month in both groups. The investigators didn't consider rate of effusion recurrence, which might help explain why the ideal group wasn't treated sooner; they might not have needed it. The higher number of ED visits in the nonideal group suggests that they may have had quicker recurrences, and should have been treated sooner, Dr. Gonzalez said.

The patients were 70 years old, on average, and about 60% were women. Lung and breast were the most common cancers.

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believe our patients should have no sleepless nights,” Dr. Mattingley said.

There's usually not much tissue left after genetic work-up to send into a clinical trial, but using blood to identify mutations “may allow us to conserve our tissue block for future trials,” noted Dr. Mattingley, who is a speaker for GeneStrat's maker, Biodesix.

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## VIEW ON THE NEWS

**M. Patricia Rivera, MD, FCCP,**

**comments:** The results of this study are very promising. The high concordance between liquid biopsies and tissue biopsies as well as the short turnaround time for the results of the liquid biopsies makes a big difference in terms of getting patients started on appropriate therapy sooner rather than later. We need additional studies to find out if liquid biopsies will be good for detection of other molecular alterations such as ROS-1 and EGFR acquired mutation T790M.



## Counseling, shared decision-making visit boosts knowledge of lung cancer risks

BY JIM KLING  
Frontline Medical News

FROM CHEST

**A** counseling and shared decision-making visit improved patient knowledge of the eligibility criteria, benefits, and potential risks of lung cancer screening via a low-radiation chest CT scan.

The Centers for Medicare & Medicaid Services has added the type of visit addressed in this study to Medicare's preventive services benefits for individuals meeting certain criteria, but no previous study had looked at how the implementation of such a visit impacted a patient's knowledge and understanding.

Subjects in this study were initially quizzed for knowledge about screening criteria, hazards, and benefits, and then underwent the counseling program. They were tested again immediately after the session, and then 1 month later.

The researchers noted significant improvement in all questions before and after a counseling session ( $P = .03$  to  $P$  less than .0001). Those improvements lessened at 1 month, but were still higher than precounseling scores.

The percentages of participants who knew the age criteria for lung cancer screening before counseling, immediately after counseling, and 1 month after counseling, for example, were 8.8% (11 patients), 59.2% (74 patients), and 21.4% (24 patients), respectively. The percentage of participants able to identify at least one of the potential hazards of screening increased by a similar amount immediately after receiving counseling, as did the percentage of participants able to identify the age criteria for lung cancer screening immediately after receiving counseling. The percentages of patients able to identify at least one of the potential hazards of screening were 38.4% before counseling and 90.4% immediately after receiving counseling. One month following counseling, the percentage of patients with such knowledge remained fairly high, dropping to 78.6%.

The researchers developed a centralized counseling and shared decision-making visit that included a narrated slide show and individualized risk assessment. They approached 423 consecutive patients who had been identified by their primary care provider or a specialist as potential candidates for screen-

ing. Of those 423 patients, 125 agreed to participate in the study (Chest. 2016 Nov 1. doi: 10.1016/j.chest.2016.10.027).

The session delivered expected improvements in patient knowledge, but there were some surprises. “The starting point of knowledge was perhaps less than we would have anticipated, and the gains, though very substantial, weren't perfect,” said Peter J. Mazzone, MD, MPH, FCCP, who led the study, in an interview.

The drop in knowledge at 1 month suggests that the information needs to be reinforced, possibly each time patients come in for an annual screening visit, added Dr. Mazzone, who is also director of the lung cancer screening program at the Cleveland Clinic.

Counseling sessions can also help convince patients to quit smoking, if tobacco use is a concern. “It's not appropriate to screen for lung cancer without making a commitment to try to quit,” said David Grossman, vice chair of the US Preventive Services Task Force and a senior investigator at the Group Health Research Institute, Seattle, in an interview.

This story's sources reported no financial disclosures.

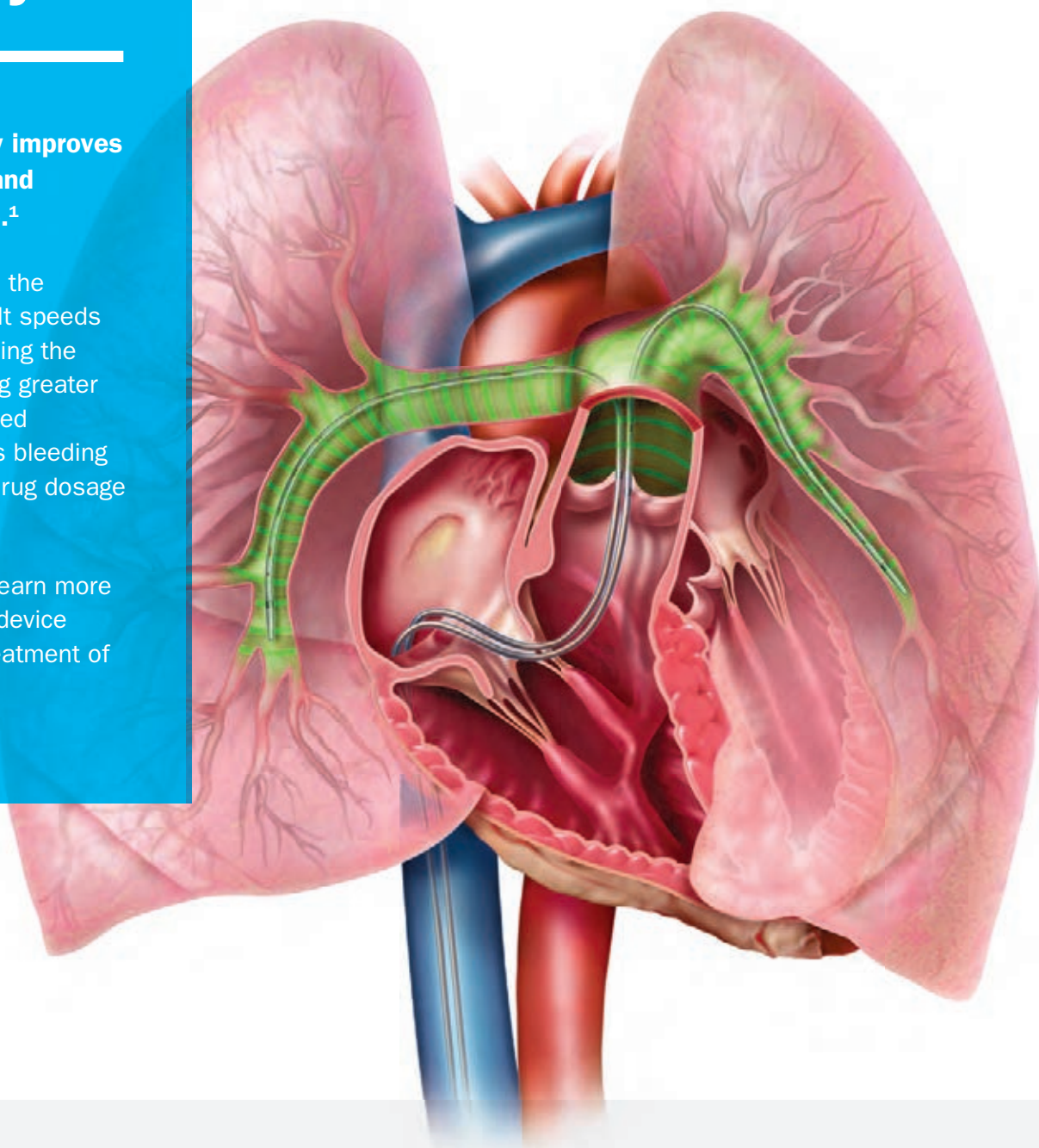


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<sup>2</sup> Braaten, J et al., *Thromb Haemost* 1997;78:1063-8; Francis, C et al. *Ultrasound in Medicine and Biology* 1995; 21(3):419-424; Soltani, A et al., *Physics in Medicine and Biology* 2008; 53:6837-6847

<sup>3</sup> Kucher, N., et al., *Circulation*, Vol. 129, No. 4, 2014, 479–486.

<sup>4</sup> Piazza, G., et al., *American College of Cardiology 63rd Annual Scientific Session, Wash D.C., March 30, 2014.*

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