From PERT to AI, care for high-risk pulmonary emboli evolves

BY RICHARD MARK KIRKNER
MDedge News

In 2012, a small group of specialists met to Monday morning quarterback an acute pulmonary embolism case that didn’t go as well as they’d hoped. The specialists, consisting of a critical care pulmonologist, cardiologist, cardiac surgeon, and vascular specialist, at Massachusetts General Hospital, Boston, came up with a concept known as the pulmonary embolism response team – PERT for short – an idea that soon took hold in other centers and served as the vanguard to other innovative approaches to managing critical care patients with PE, which is the third-leading cause of cardiovascular death in the United States (Intern Emerg Med. 2023. doi: 10.1007/s11739-022-03180-w).

Three years later the PERT Consortium came together, and today it has 102 members, according to the organization’s website (pertconsortium.org), including members in South America, Europe, Asia, and Australia. Since then, PE strategies have evolved to target mental health issues recovering patients have, improve follow-up after discharge, and even investigate artificial intelligence and apps to expedite diagnosis and treatment. The PERT Consortium, meanwhile, is in the process of creating the PE Centers of Excellence program to certify centers that meet certain requirements.

DASH diet found to affect lung function, risk of COPD

BY HEIDI SPLETE
MDedge News

Greater adherence to the Dietary Approaches to Stop Hypertension (DASH) diet was associated with a significantly reduced risk of chronic obstructive pulmonary disease (COPD) and improved lung function, based on data from more than 28,000 individuals in the United States.

Diet is a modifiable risk factor for COPD and other chronic diseases, but the effects of specific diet models such as the DASH diet and Mediterranean diet on COPD in particular has not been well studied, Jingli Wen, MD, of Nanjing Medical University, Jiangsu, China, and colleagues wrote.

In a study published in Frontiers in Nutrition (2023 Feb 2. doi: 10.3389/fnut.2023.1031071), the researchers reviewed data from 28,605 adult participants in the National Health and Nutrition Examination Survey from 1999 to 2018. The study population included 2,488 individuals with COPD and 25,607 individuals without.

DASH // continued on page 6

CHEST SEEK™ Library Plus

+1,200 questions and +300 CME/MOC/CE

SUBSCRIBE NOW
COPD; the mean ages of the COPD and non-COPD groups were 60.2 years and 56.9 years, and the proportion of women was 63.7% and 51.4%, respectively. The primary outcome was the prevalence of COPD, defined as self-reports of a diagnosis of chronic bronchitis or emphysema. DASH diet scores were based on consumption of nine target nutrients: saturated fat, total fat, protein, cholesterol, fiber, magnesium, calcium, potassium, and sodium. Scores for compliance with the Mediterranean diet were based on intake of eight food categories: fruits, vegetables, legumes, fish, red meat, dairy products, alcohol, and olive oil.

Overall, a higher score for adherence to the DASH diet was significantly associated with a lower COPD risk (odds ratio, 0.83; P = 0.021). This association remained significant in subgroups of younger adults (OR, 0.74), men (OR, 0.73), and smokers (OR, 0.82).

By contrast, adherence to the Mediterranean diet was not significantly associated with COPD prevalence (OR, 1.03; P = 0.697). A review of cross-sectional studies noted that dietary practices vary across regions, and the cross-sectional design prevents conclusions of causality.

The study findings were limited by several factors including the cross-sectional design that prevented conclusions of causality, the researchers noted. Other limitations included the lack of data of the impact of poor living habits, such as smoking, on food decisions, the use of short-term 24-hour dietary recall, and the reliance of self-reports for a diagnosis of COPD.

However, the results support the role of diet in COPD pathogenesis. More prospective studies and clinical intervention studies are needed, but the findings should encourage clinicians to consider the potential role of a healthy diet in promoting lung health. The study was supported by the Department of Health, Jiangsu Province, China. The researchers had no financial conflicts to disclose.

The researchers also found a correlation between DASH diet adherence and improved lung function, especially among individuals without COPD. DASH focuses on low sodium, whole grains, and fresh fruits and vegetables.

The researchers also found a correlation between DASH diet adherence and improved lung function, especially among individuals without COPD.
“Part of the reason we recognized that a discussion across specialties was important was because there weren’t the large clinical trials that could tell us exactly what to do for any given case,” said Christopher Kabrhel, MD, MPH, director of the Center for Vascular Emergencies at Mass General and a professor at Harvard Medical School in Boston, who assembled that formative meeting. “Without a clear basis in data, it was really important to have all the different specialists weigh in and give their perspective and talk about what was the best approach for the patient’s care.”

Filling data gaps
Some of those data gaps persist today, Dr. Kabrhel said. “It’s precisely that lack of head-to-head data that existed in 2012, and to a great extent still exists today, that led us to create this system.” The American Heart Association just this January issued a scientific statement on survival in high-risk PE—carefully laid out a plan for how to approach these patients. “The American Heart Association just this January issued a scientific statement on survival in high-risk PE—carefully laid out a plan for how to approach these patients.”

Evolving to follow-up care
As the PERT protocol led to better inpatient outcomes, the teams became more aware that discharged PE patients were struggling with mental health and other quality-of-life issues—symptoms that have been understudied, according to a recent study in the Journal of Cardiovascular Disease. A recent study in the Journal of Cardiovascular Disease.

The University of Pittsburgh Medical Center PERT has started evaluating artificial intelligence to aid in PE diagnosis. Belinda Rivera-Lebron, MD, director of the acute and chronic embolism program at Pitt, explained that the AI protocol hasn’t been adopted yet, but the concept is to have a platform that’s compatible with the hospital system’s electronic medical record.

She described how AI would work once the PERT is activated. “Once the patient goes through the CT scan, within 60 seconds of that scan being completed, the scan gets uploaded into the cloud and the app or the platform is able to tell you whether there is PE present or absent, and whether there is right-ventricle dilatation on that scan. This is even before you probably even think about opening up the computer to look at the scan, and even before radiology opens up the scan to read,” she said. “It’s so fast.”

The idea is to send the scans rapidly to the PERT. “It will send you a text, a notification on your phone that will tell you Mr. Smith is PE positive,” Dr. Rivera-Lebron said. “Then you open it and you are able to scroll through the CT scan in your phone. So, it’s really remarkable.”

Clinical trials worth watching
Meanwhile, a number of clinical trials have started to enroll patients, or will soon, that Dr. Rivera-Lebron said are worth paying attention to. PEITHO-3 is a randomized, placebo-controlled trial with long-term follow-up comparing the efficacy of PEITHO-3 is a randomized, placebo-controlled trial with long-term follow-up comparing the efficacy of
NEWS

‘Unheard-of’ PAH improvement seen with novel drug

BY MITCHEL L. ZOLER, PHD
MDedge News

NEW ORLEANS – An investigational, first-in-class agent that delivers a completely new type of intervention to patients with pulmonary arterial hypertension (PAH) scored a clear win in the STELLAR trial, the first to complete among three phase 3 trials that are testing this agent.

Sotatercept, administered subcutaneously every 3 weeks for 24 weeks, improved from baseline average 6-minute walk distance (6MWD) by a significant and clinically meaningful 40.8 meters, compared with placebo, for the trial’s primary efficacy endpoint (P < .001). The treatment also “delivered broad clinical benefit across multiple domains including hemodynamics, World Health Organization functional class, disease biomarkers, risk scores, and patient-reported outcomes,” Marius M. Hoepner, MD, said at the joint scientific sessions of the American College of Cardiology and the World Heart Federation.

“These results establish the clinical utility of sotatercept, administered in combination with approved PAH therapies, as a new treatment for PAH,” added Dr. Hoepner, professor and deputy director of the department of respiratory medicine at Hannover (Germany) Medical School.

“The most important aspect was the hemodynamic improvement,” with sotatercept treatment, which led to an average 235 dyn/sec per cm−5 reduction in pulmonary vascular resistance from baseline and an average cut in pulmonary artery pressure of 13.9 mm Hg from baseline, compared with placebo, a result that is “unheard of,” Dr. Hoepner said in a press conference during the meeting.

“With other tested agents we usually see very little improvement in pulmonary artery pressure. This is a signal that we achieved some reversing of the pathological changes in the pulmonary vessels that lead to PAH, he added.


‘A new hope’ for patients with PAH

Based on the reported findings, sotatercept is a “very exciting boutique molecule” that will “offer patients with PAH a very exciting new treatment,” commented Rhonda Cooper-DeHoff, PharmD, a designated discussant and a researcher at the University of Florida, Gainesville.

“This study is a new hope for patients with PAH. Until now, they’ve had really bad outcomes, but [in this study] we see significant differences in 6MWD, hemodynamics, and risk factors. Overall, I think the benefit is greater than the risk. “It may pose to patients through potential adverse effects, commented Julia Grapsa, MD, PhD, a cardiologist at St. Thomas Hospital in London, and another discussant at the meeting.

“The results are impressive” and “encouraging,” and “suggest that sotatercept may represent a new and clinically consequential addition to current medications for PAH,” wrote three clinicians from Canyons Region Intermountain Medical Center in Murray, Utah, in an editorial that accompanied the published report (N Engl J Med. 2023 Mar 6. doi: 10.1056/NEJMe2300324).

But the authors of the editorial also raised several cautions and concerns.

They questioned the generalizability of the findings, noting that the patients with PAH enrolled in the study were all adults who were clinically stable and an average of more than 8 years out from their initial PAH diagnosis, and more than 90% were on stable treatment for PAH with two or three agents specific for treating the disorder.

The study cohort also had a disproportionately high enrollment of patients with idiopathic (59%) disorders.

Until now, they’ve had really bad outcomes, but [in this study] we see significant differences in 6MWD, hemodynamics, and risk factors. Overall, I think the benefit is greater than the risk. “It may pose to patients through potential adverse effects, commented Julia Grapsa, MD, PhD, a cardiologist at St. Thomas Hospital in London, and another discussant at the meeting.

The study cohort also had a disproportionately high enrollment of patients with idiopathic (59%) or heritable (18%) forms of PAH, and the 15% of patients in the trial with connective tissue disease represented a disproportionally low prevalence of this PAH subtype.

The editorialists also called for “ongoing vigilance” for adverse effects from sotatercept treatment, although they acknowledged that the adverse effects reported to date from sotatercept are “largely reassuring.”

Death or clinical worsening cut by 84%

STEELLAR randomized 323 patients at 91 sites in 21 countries with WHO Group 1 PAH and with WHO functional class II or III disease to receive either sotatercept or placebo for 24 weeks, with an option for treatment to continue beyond that until the last patient in the study reached 24 weeks on treatment, resulting in an overall median treatment duration of nearly 33 weeks.

In addition to the significant result for the primary endpoint, the 163 patients who received sotatercept had significant improvements, compared with 160 placebo-treated patients, for eight of nine secondary endpoints. The only secondary endpoint with a neutral result was for a measure of cognitive and emotional wellbeing, a parameter that was already at a normal level at baseline in most enrolled patients, Dr. Hoepner explained.

The incidence of either death or an event indicative of clinical worsening during the overall median follow-up of almost 33 weeks was 26.3% among the control patients and 5.5% among those who received sotatercept. This translated into a significant reduction for this endpoint of 84% with sotatercept treatment, compared with placebo.

The rates of treatment-emergent adverse events leading to discontinuation were roughly the same in the control and sotatercept arms, and the incidence of severe or serious treatment-emergent adverse events was higher among the control patients.

The most common adverse event on sotatercept was bleeding events, which occurred in 32% of those on sotatercept and in 16% of the control patients, but the events in the sotatercept arm were “mostly mild,” said Dr. Hoepner. The next most frequent adverse event during sotatercept treatment was appearance of telangectasias, which occurred in 14% of those on sotatercept and in 4% of control patients.

“It’s an uncommon adverse event profile, but not unexpected for a drug with its mechanism of action,” he said.

Drug binds activin, a pathologic driver of PAH

Sotatercept is an engineered molecule that combines a section of a human immunoglobulin G molecule with a portion of the receptor for activin. This structure allows sotatercept to bind free activin molecules in a patient’s blood, thereby removing a key driver of the pulmonary vascular wall remodeling that is at the pathologic root of PAH.

Dr. Ardeshna and Dr. Tefera have no relevant relationships to disclose. Dr. Rivera-Lebron disclosed relationships with INARI Catheter and Johnson & Johnson.

Dr. Kabrhel disclosed relationships with Bristol Myers Squibb and Pfizer.
Are childhood viral infections linked with asthma?

BY NATHALIE RAFFIER

MARSEILLE, FRANCE – It is well known that viral infections, especially respiratory syncytial virus (RSV) and rhinovirus (RV), exacerbate symptoms of asthma. But could they also play a part in triggering the onset of asthma?

The link between RSV and RV infections in early childhood and the development of asthma symptoms is well established, said Camille Taillé, MD, PhD, of the department of respiratory medicine and the rare diseases center of excellence at Bichat Hospital, Paris. But getting asthma is probably not just a matter of having a viral infection at a young age or of having a severe form of it. Gene polymorphisms, immune system disorders, and pre-existing atopy are also associated with the risk of asthma. This was the focus of the 27th French-language respiratory medicine conference, held in Marseille, France.

RV and RSV

Persons with asthma are vulnerable to certain viral respiratory infections, in particular the flu and RV, which can exacerbate asthma symptoms. Inhaled corticosteroids have an overall protective effect against viral-induced exacerbations. For worsening asthma symptoms during an epidemic or pandemic, there is no contraindication to inhaled or oral corticosteroids.

Young children from the time of birth to 4 years of age are particularly susceptible to viral respiratory infections. According to data from France’s clinical surveillance network, Sentinelles, from the period covering winter 2021-2022, the rate of incidence per 100,000 inhabitants was systematically greater for the 0 to 4-year age range than for older age ranges.

Of the most common viruses that infect young children, RV, the virus that causes the common cold, is a nonenveloped RNA virus from the enterovirus family. The virus is highly variable, which makes developing a vaccine challenging. The virus circulates year round, usually peaking in the fall and at the end of spring. RSV is an RNA virus that is classified as a respiratory virus. Almost all children will have been infected with RSV by the time they are 2 years old.

Epidemics occur each year during winter or in early spring in temperate climates. Vaccines are currently being developed and will soon be marketed. A monoclonal antibody (palivizumab), which targets fusion proteins of the virus, is available as prophylactic treatment for at-risk children.

During an RSV infection, the severe inflammation of the bronchial and alveolar walls causes acute respiratory distress. “But not all infants will develop severe forms of bronchiolitis,” said Dr. Taillé. “The risk factors for the severe form of the illness are well known: being under 6 months of age, prematurity, comorbidities (neurovascular, cardiovascular, respiratory, etc.), history of a stay in a neonatal intensive care unit at birth, living in low socioeconomic status towns, and exposure to smoking.”

Asthma development

The issue of whether or not viral diseases cause asthma has been the subject of intense debate. The studies are starting to stack up, however. They seem to show that RSV or RV infections are associated with the risk of subsequent asthma development. “For example, in a study published in 2022,” said Dr. Taillé, “in children admitted with an RSV infection, 60% of those who had been admitted to neonatal intensive care presented with symptoms of asthma between 3 and 6 years of age, compared with 18% of those who had had a milder case of RSV (admitted to nonintensive care settings). A serious RSV infection is a risk factor for later development of asthma.”

However, the link between RSV and later onset of asthma is also seen in milder cases of the infection. The American COAST study was designed to examine the effect of childhood respiratory infections on the risk of developing asthma. Researchers followed 259 newborns prospectively for 1, 3, and 6 years.

“You now know that RSV is not the only pathogen responsible for bronchiolitis. RV is often found, now that it can routinely be detected by PCR tests,” said Dr. Taillé. In the COAST study, the onset of wheezing during an RSV or RV infection in children aged 0-3 years was associated with an increased risk of asthma at 6 years of age. Globally, 28% of children infected by either virus were deemed to have asthma at 6 years of age. “There is clearly a link between having had a respiratory virus like RV or RSV and getting asthma symptoms at 6 years of age,” said Dr. Taillé. “What’s more, the effect of RV is not changed in this study by allergic sensitization.”

The results of cohort studies, from several countries are consistent with each other: Persons who have contracted RV or RSV are more likely to suffer from recurrent wheezing or asthma, especially if the infection is contracted in infancy or if it is severe. “Some studies even suggest that viral-induced asthma is more severe,” said Dr. Taillé. “For example, a Scottish study (2020. doi: 10.1002/ppul.24676) ... showed that children with a previous history of RSV infection had more hospital admissions and required more medication than asthmatics with no history of an RSV infection, suggesting the link between a previous history of RSV infection and the development of a more severe form of asthma.”

A 2023 study (doi: 10.1016/j. rmmed.2022.107062) of the effects of respiratory illnesses in childhood evaluated lung structure and function via CT scans of 39 patients aged 26 years and concluded that participants who had been infected with RSV in childhood presented with increased air trapping, which is suggestive of airway abnormalities, possibly linked to a direct effect of viruses on lung development.

Mechanisms of action

“The real question is understanding if it’s the virus itself that causes asthma, or if the virus is simply uncovering underlying asthma in predisposed children,” said Dr. Taillé. From 30% to 40% of children who have had RSV will go on to develop wheezing or asthma in childhood. This observation suggests that there are factors favoring the development of asthma after infection with RSV.

RV is thought to be associated with the development of asthma and wheezing, especially in people with a preexisting atopy or a reduced interferon immune response, while RSV, which occurs at a younger age and among the most vulnerable populations, seems to act independently of a person’s predisposition to allergies. RV stands out from other viral factors, owing to its tendency to create a Th2-biased inflammatory environment and its association with specific risk genes in people predisposed to asthma development (CDHR3).

Dr. Taillé has disclosed no relevant financial relationships.
Diabetes drug may help prevent long COVID according to early research study

BY CAROLYN CRIST

Metformin appears to play a role in preventing long COVID when taken early during a COVID-19 infection, according to preprints with The Lancet on SSRN. The preprint hasn’t yet been peer-reviewed or published in a journal.

In particular, metformin led to a 42% drop in long COVID among people who had a mild to moderate COVID-19 infection. “Long COVID affects millions of people, and preventing long COVID through a treatment like metformin could prevent significant disruptions in people’s lives,” said lead author Carolyn Bramante, MD, assistant professor of internal medicine and pediatrics at the University of Minnesota, Minneapolis.

Between January 2021 and February 2022, Dr. Bramante and colleagues tested three oral medications – metformin (typically used to treat type 2 diabetes), ivermectin (an antiparasitic), and fluvoxamine (an antidepressant) – in a clinical trial across the United States called COVID-OUT. The people being studied, investigators, care providers, and others involved in the study were blinded to the randomized treatments. The trial was decentralized, with no in-person contact with participants.

The researchers included patients who were aged 30-85 with overweight or obesity, had documentation of a confirmed COVID-19 infection, had fewer than 7 days of symptoms, had no known prior infection, and joined the study within 3 days of their positive test. The study included monthly follow-up for 300 days, and participants indicated whether they received a long COVID diagnosis from a medical doctor, which the researchers confirmed in medical records after participants gave consent.

The medications were prepackaged into pill boxes for fast delivery to participants and to ensure they took the correct number of each type of pill. The packages were sent via same-day courier or overnight shipping.

The metformin doses were doled out over 14 days, with 500 milligrams on the first day, 500 milligrams twice a day for the next 4 days, and then 500 milligrams in the morning and 1,000 milligrams in the evening for the remaining 9 days.

“With the burden of long COVID on society, confirmation is urgently needed in a trial that addresses our study’s limitations in order to translate these results into practice and policy.”

Among the 1,323 people studied, 1,125 agreed to do long-term follow-up for long COVID: 564 in the metformin group and 561 in the blinded placebo group. The average age was 45, and 56% were women, including 7% who were pregnant.

The average time from the start of symptoms to starting medication was 5 days, and 47% began taking the drug within 4 days or less. About 55% had received the primary COVID-19 vaccination series, including 5.1% who received an initial booster, before enrolling in the study.

Overall, 8.4% of participants reported that a medical provider diagnosed them with long COVID. Of those who took metformin, 6.3% developed long COVID, compared to 10.6% among those who took the identical-matched placebo.

The risk reduction for metformin was 42% versus the placebo, which was consistent across subgroups, including vaccination status and different COVID-19 variants. When metformin was started less than 4 days after COVID-19 symptoms started, the effect was potentially even greater, with a 64% reduction, as compared with a 36% reduction among those who started metformin after 4 or more days after symptoms.

Neither ivermectin nor fluvoxamine showed any benefits for preventing long COVID. At the same time, the study authors caution that more research is needed.

“The COVID-OUT trial does not indicate whether or not metformin would be effective at preventing long COVID if started at the time of emergency department visit or hospitalization for COVID-19, nor whether metformin would be effective as treatment in persons who already have long COVID,” they wrote. “With the burden of long COVID on society, confirmation is urgently needed in a trial that addresses our study’s limitations in order to translate these results into practice and policy.”

Several risk factors for long COVID emerged in the analysis. About 11.1% of the women had a...
Even mild COVID is hard on the brain

BY MEGAN BROOKS

Even mild cases of COVID-19 can affect the function and structure of the brain, early research suggests.

“Our results suggest a severe pattern of changes in how the brain communicates as well as its structure, mainly in people with anxiety and depression with long-COVID syndrome, which affects so many people,” study investigator Clarissa Yasuda, MD, PhD, from University of Campinas, São Paulo, said in a news release.

“The magnitude of these changes suggests that they could lead to problems with memory and thinking skills, so we need to be exploring holistic treatments even for people mildly affected by COVID-19,” Dr. Yasuda added.

The findings were released March 6 ahead of the study’s scheduled presentation at the annual meeting of the American Academy of Neurology.

Brain shrinkage

Some studies have shown a high prevalence of symptoms of anxiety and depression in COVID-19 survivors, but few have investigated the associated cerebral changes, Dr. Yasuda told this news organization.

The study included 254 adults (177 women, 77 men, median age 41 years) who had mild COVID-19 a median of 82 days earlier. A total of 102 had symptoms of both anxiety and depression, and 152 had no such symptoms.

On brain imaging, those with COVID-19 and anxiety and depression had atrophy in the limbic area of the brain, which plays a role in memory and emotional processing.

No shrinkage in this area was evident in people who had COVID-19 without anxiety and depression or in a healthy control group of individuals without COVID-19.

The researchers also observed a “severe” pattern of abnormal cerebral functional connectivity in those with COVID-19 and anxiety and depression.

In this functional connectivity analysis, individuals with COVID-19 and anxiety and depression had widespread functional changes in each of the 12 networks assessed, while those with COVID-19 but without symptoms of anxiety and depression showed changes in only five networks.

Mechanisms unclear

“Unfortunately, the underpinning mechanisms associated with brain changes and neuropsychiatric dysfunction after COVID-19 infection are unclear,” Dr. Yasuda told this news organization.

“Some studies have demonstrated an association between symptoms of anxiety and depression with inflammation. However, we hypothesize that these cerebral alterations may result from a more complex interaction of social, psychological, and systemic stressors, including inflammation. It is indeed intriguing that such alterations are present in individuals who presented mild acute infection,” Dr. Yasuda added.

“Symptoms of anxiety and depression are frequently observed after COVID-19 and are part of long-COVID syndrome for some individuals. These symptoms require adequate treatment to improve the quality of life, cognition, and work capacity,” she said.

Treating these symptoms may induce “brain plasticity, which may result in some degree of gray matter increase and eventually prevent further structural and functional damage,” Dr. Yasuda said.

A limitation of the study was that symptoms of anxiety and depression were self-reported, meaning people may have misjudged or misrepresented symptoms.

Commenting on the findings for this news organization, Cyrus Raji, MD, PhD, with the Mallinckrodt Institute of Radiology, Washington University, St. Louis, said the idea that COVID-19 is bad for the brain isn’t new. Dr. Raji was not involved with the study.

Early in the pandemic, Dr. Raji and colleagues published a paper detailing COVID-19’s effects on the brain (J Alzheimers Dis. 2020 Jun 30. doi: 10.3233/JAD-200581), and Dr. Raji followed it up with a TED talk on the subject (www.youtube.com/watch?v=zCfKNdq2CEg&t=325s).

“Within the growing framework of what we already know about COVID-19 infection and its adverse effects on the brain, this work incrementally adds to this knowledge by identifying functional and structural neuroimaging abnormalities related to anxiety and depression in persons suffering from COVID-19 infection,” Dr. Raji said.

The study was supported by the São Paulo Research Foundation. The authors have no relevant disclosures. Raji is a consultant for Brainreader, Apollo Health, Pacific Neuroscience Foundation, and Neurevolution LLC.
Changes in COPD nomenclature; melioidosis in the U.S.; air quality monitors; and more ...

**AIRWAYS DISORDERS NETWORK**

**Asthma & COPD Section**

2023 GOLD update: Changes in COPD nomenclature and initial therapy

The 2023 GOLD committee proposed changes in nomenclature and therapy for various subgroups of patients with COPD. The 2023 GOLD committee changed the ABCD group classification to ABE (for exacerbations), which highlights the importance of the number and severity of exacerbations irrespective of daily symptoms.

The mainstay of initial treatment for symptomatic COPD should include combination LABA/LAMA bronchodilators in a single inhaler. For patients with features of concomitant asthma or eosinophils greater than or equal to 300 cells/µl, an ICS/LABA/LAMA combination inhaler is recommended.

People with "young COPD" develop respiratory symptoms and meet spirometric criteria for COPD between the ages of 25 and 50 years old. Other terminology changes center around those with functional and/or structural changes suggesting COPD, but who do not meet the post-bronchodilator spirometric criteria to confirm the COPD diagnosis. Those with "pre-COPD" have normal spirometry, including the FEV₁ and FEV₁/FVC ratio, but have functional and/or structural changes concerning for COPD. Functional changes include air trapping and/or hyperinflation on PFTs, low diffusion capacity, and/or decline in FEV₁ of >40 mL per year.

Structural changes include emphysematous changes and/or bronchial wall changes on CT scans. "PRISm" stands for pre-served ratio with impaired spirometry, where the postbronchodilator FEV₁/FVC is greater than or equal to 0.70, but FEV₁ is < 80% predicted with similar functional and/or structural changes to those with "pre-COPD." People with PRISm have increased all-cause mortality. Not all people with pre-COPD or PRISm progress clinically and spirometrically to COPD; however, they should be treated because they have symptoms as well as functional and/or structural abnormalities. Despite increasing data regarding pre-COPD and PRISm, many gaps remain regarding optimal management.

**REFERENCE**


**CHEST INFECTIONS & DISASTER RESPONSE NETWORK**

**Disaster Response & Global Health Section**

Closer to home: Melioidosis in the United States

Global travel and climatic changes are changing the boundaries for diseases once considered to be geographically limited. Melioidosis, caused by the gram-negative bacterium Burkholderia pseudomallei, does not usually appear on the differential diagnosis of patients in the United States. Historically endemic to South and Southeast Asia, Australia, Puerto Rico, and Central America, B. pseudomallei infects humans via direct inoculation of the skin, through inhalation, or by the ingestion of contaminated soil or water. Importation of melioidosis to the United States from civilian travelers, global commerce, or military personnel is becoming more common (Cee JE, et al. N Engl J Med. 2012;367[11]:1035).

**DIFFUSE LUNG DISEASE & LUNG TRANSPLANT NETWORK**

**Occupational & Environmental Health Section**

Use of low-cost air quality monitors for patients with lung disease

The World Health Organization estimates significant air pollution-attributable deaths, including 11% of lung cancer deaths, 18% of COPD deaths, and 23% of pneumonia deaths (https://www.who.org). Many pulmonologists recommend minimizing air pollution exposure to reduce the development and progression of lung diseases (Carlsten C, et al. Eur Respir J. 2020;55[6]:1902056).

The Environmental Protection Agency uses air quality (AQ) monitors around the country to track ambient pollutant levels. These real-time data are available to the public on AirNow.gov; however, these data do not reflect indoor air pollutants. Thus, AQ monitors may not accurately represent the total air pollution exposure to patients.

Low-cost AQ monitors available for purchase enable indoor AQ monitoring.

Unfortunately, many indoor air pollutants do not have well-established safe levels. Although several devices detect specific pollutants like volatile oxygen compounds or particulate matter, other harmful compounds may remain undetectable and unmonitored. Even if high pollutant levels are detected, most devices are not designed to alarm like smoke and carbon monoxide detectors (https://www.epa.gov).

Although efficacy data are limited, several laboratories, such as the Indoor Environment Lab at Berkeley, have conducted performance evaluations. In a study of 16 devices publicly available for purchase, the devices tended to underreport pollutant levels by nearly 50%. Nevertheless, most devices successfully detected the presence of pollutants (Demanega et al. Environmental Monitoring and Assessment. 2022;194[5]:12).
NEWS FROM CHEST

Regardless of these limitations, low-cost AQ monitors may empower patients to intervene on unsafe household conditions and minimize their risk of poor lung health.

Alexys Monoson, MD
Section Fellow-in-Training
Sean Callahan, MD
Section Member-at-Large
Bathmapriya Balakrishnan, MD,
FCCP - SectionVice Chair

PULMONARY VASCULAR & CARDIOVASCULAR NETWORK Cardiovascular Medicine & Surgery Section
Training the future cardiac intensivist to meet the demands of the modern cardiovascular ICU
Over the recent decades, the cardiovascular intensive care unit (CICU) has seen a significant transformation. Not only has the acuity of cardiac conditions evolved, but the prevalence of non-cardiac critical illness has multiplied (Yuriditsky E, et al. ATS Sch. 2022;3[4]:522).
The tradition of general cardiologists managing CICUs was believed to be an unsustainable model and, in 2012, the American Heart Association (AHA) published a scientific statement detailing pathways to train cardiologists in critical care medicine (CCM) (Morrow DA, et al. Circulation. 2012;126:1408).
However, fewer than 15% of modern CICUs are staffed by physicians dual-boarded in cardiology and CCM; most believe that CCM training is necessary to effectively practice in the CICU (van Diepen S, et al. Circ Cardiovasc Qual Outcomes. 2017;10:e003864).
How best do we develop future cardiac intensivists to manage complex decompensated cardiovascular disease with compounded medical critical illness?
Multiple training pathways leading to board eligibility and dual certification have been outlined (Geller BJ, et al. J Am Coll Cardiol. 2018;72:1171).
A commonly elected path requires the completion of a 1-year CCM fellowship following a 3-year general cardiology fellowship.
As few programs exist, limited guidance is available surrounding CCM fellowship design for the cardiologist; however, proposed curricula have been published (Yuriditsky E, et al. ATS Sch. 2022;3[4]:522).
Developing such programs requires collaboration between cardiologists and intensivists to secure funding, develop infrastructure, obtain accreditation, and to recruit candidates.
Having completed dual training, I not only saw my skillset flourish, but the partnership between CCM and cardiology strengthen.
Eugene Yuriditsky, MD
Section Fellow-in-Training

In memoriam

CHEST has been informed of the following deaths of CHEST members. We remember our colleagues and extend our sincere condolences.

Stephen P. Bradley, MD
Krishan K. Goyle, MD, FCCP
J. Randall Curtis, MD
Echocardiography for the Cardiac Anesthesiologist

By John K. Zakrzewski, MD

Echocardiography (ECHO) is an essential component of cardiac anesthesia. It allows for real-time visualization of the heart and great vessels, providing critical information during perioperative and anesthesia management. This review will focus on the use of ECHO in the cardiac anesthesiologist's practice, with a particular emphasis on its role during anesthesia and surgery.

Key Points:
- Understanding the anatomy and function of the heart and great vessels
- Recognizing normal and abnormal echocardiographic findings
- Utilizing ECHO to guide anesthesia and surgical procedures

The use of echocardiography in cardiac anesthesia is crucial for ensuring patient safety and optimizing outcomes. It is a dynamic and integral part of the cardiac anesthesiologist's toolkit, allowing for a comprehensive approach to patient care.

Prepare to pass with CHEST Board Review

Whether you’re a graduating fellow or an accomplished physician, preparing for board exams can be challenging. That’s why the experts recommend starting slow and setting reasonable expectations for every step of the process.

“I think starting as early as you can is one way to make it less daunting,” said Meredith Pugh, MD, MSCI, Critical Care Board Review 2023 Vice-Chair.

Give yourself a 6-month timetable, and focus on tackling one topic or chapter at a time. Increase the length of your study sessions and the amount of material to review over time, building on your knowledge base with repetition and continuous reinforcement. And, be sure to celebrate every new lesson learned—and continuously identify areas of opportunities—with frequent knowledge checks.

To take your prep to the next level, our faculty recommend getting assistance from the experts (and a few friends) at CHEST Board Review.

**Capitalize on the curriculum**

Attend CHEST Board Review to tackle knowledge gaps with the assistance of expert faculty, share study tips and techniques with your peers, and get a better understanding of what to expect on test day with a curriculum designed around the board exams. Three live, in-person courses are offered this year, covering pulmonary medicine, sleep medicine, and critical care medicine.

The Sleep Medicine Board Review and Pulmonary Medicine Board Review courses offer the opportunity to tackle exam content step-by-step. Learn from global experts as they cover key exam topics found on the ABIM blueprints.

This year, the Critical Care Medicine Board Review course will offer a slightly different format—but the same exam-focused curriculum—by concentrating on knowledge review on site. Learners will receive recorded lectures in advance, so that time in Miami is spent on case-based discussions and Q&A with faculty and other learners. Registration for CHEST Board Review in Miami is now open. Save your spot today at www.chestnet.org/Learning-and-Events/Events/Board-Review.

- **Sleep Medicine Board Review:** August 9-11
- **Critical Care Medicine Board Review:** August 12-14
- **Pulmonary Medicine Board Review:** August 16-19

---

**ECMO for refractory asthma exacerbations**

By Jonathan K. Zakrzewski, MD; Arun Kannappan, MD; and R. William Vandivier, MD

The overnight shift in the MICU began as it does for many intensivists, by hearing about ED admissions, transfers from outside hospitals, sick floor patients, and high-risk patients in the MICU. Earlier in the day, the MICU team had admitted a 39-year-old woman with a severe asthma attack that required endotracheal intubation and mechanical ventilation in the ED for hypercarbic respiratory failure. After intubation, she had no audible air movement on chest exam, severe hypercarbic respiratory acidosis determined by an arterial blood gas, a clear chest radiograph, and negative findings on a respiratory viral panel.

Her family said that she had run out of her steroid inhaler a month earlier and could not afford a refill. She had been using increasing amounts of albuterol over the past week before developing severe shortness of breath on the day of admission. The ED and MICU teams aggressively treated her with high-dose inhaled albuterol, ipratropium, and IV magnesium sulfate for bronchodilation; methylprednisolone for airway inflammation; and continuous ketamine for sedation, analgesia, and bronchodilation (Rehder K, et al. *Respir Care*. 2017;62[6]:849).

Her airway pressures continued to be high despite using lung protective ventilation, so she was shifted to a permissive hypercapnia ventilation strategy using neuromuscular blockade; deep sedation, and low minute-ventilation (Laher AE, et al. *Intensive Care Med*. 2018;33[9]:491).

Two hours into the shift, the bedside nurse noted that the patient had become hypotensive. Her ventilator pressures remained stable with peak inspiratory pressures of 38-42 cm H2O, plateau pressures of 28-30 cm H2O, auto-positive end-expiratory pressure (auto-PEEP) of 10-12 cm H2O, and fractional inspiratory oxygen (FiO2) of 40%. A repeat chest radiograph showed no signs of barotrauma, but arterial blood gas values showed severe respiratory acidosis with a pH of 7.05 and a PCO2 > 100 mm Hg. Her condition stabilized when she received a continuous infusion of bicarbonate to control her acidosis and low-dose IV norepinephrine for blood pressure control. It was at that moment that the bedside nurse astutely asked whether we should consider starting ECMO for the patient, as co-author, Dr. Arun Kannappan, had done for a similar patient with asthma a month earlier. Dr. Vandivier notes, “My first response was that ECMO was not needed, because our patient had stabilized, and I had taken care of many patients like this in the past. But as I considered the situation more carefully, it was clear that any further decompensation could put our patient’s life at risk by not leaving enough time to start ECMO in a controlled setting. In short, my ‘traditional’ approach left little room for error in a patient with high ventilator pressures and hemodynamic instability.”

ECMO is a technique used to add oxygen or remove CO2 from the blood of people with different forms of respiratory failure (Fan E, et al. *Intensive Care Med*. 2016;42:712) that was first used by Hill and colleagues in 1966 for trauma-induced lung injury (VILI).

Standing at the bedside, it seemed to the authors that it was the right time to think about instituting a salvage therapy. But was there evidence that ECMO could improve survival? Were there clear guidelines for when to initiate ECMO, and was ECMO more effective than other salvage therapies such as inhaled volatile anesthetics?

Since McDonnell and colleagues first described the use of ECMO for a severe asthma exacerbation in 1981 (*Ann Thoracic Surg.* 1981;3[2]:171) ~95 articles have been published. Other than two registry studies and a recent epidemiologic study, all of these publications were case reports, case series, and...
reviews. Mikkelsen and colleagues (ASAIO J. 2009;55[1]:47) performed a retrospective, cohort study using the International Extracorporeal Life Support Organization Registry to determine whether ECMO use for status asthmaticus was associated with greater survival than the use of ECMO for other causes of respiratory failure. From 1986 through 2006, a total of 2,127 cases of respiratory failure were identified that required ECMO, including 27 for status asthmaticus and 1,233 for other causes. Their analysis showed that 83.3% of asthmatics treated with ECMO survived to hospital discharge compared to 50.8% of people treated with ECMO for respiratory failure not due to asthma, with an odds ratio (OR) of 4.86 favoring survival of asthmatics (OR = 4.86; 95% CI, 1.65–14.31, P = .004).

Yeö and colleagues (Yeö HJ, et al. Critical Care. 2017;21:297) also used the ECLS Organization Registry to measure survival to hospital discharge, complications, and clinical factors associated with in-hospital mortality for asthmatics treated with ECMO. They included 272 people treated with ECMO for asthma between 1992 and 2016, after excluding people treated with ECMO for cardiopulmonary resuscitation or cardiac dysfunction. ECMO was associated with improvements in ventilator mechanics, including a reduction in respiratory rate, Fin, peak inspiratory pressure, mean airway pressure, and driving pressure. Use of ECMO for status asthmaticus was also associated with an 83.5% survival to hospital discharge, similar to the 83.3% survival rate by Mikkelsen and colleagues. Hemorrhage, the most common complication, occurred in roughly a quarter of people treated with ECMO. In the multivariate analysis, age, bleeding, pre-ECMO PEEP, post-ECMO Fin, and driving pressure were all associated with higher in-hospital mortality.

Although there are no formal criteria to guide use of ECMO for asthma exacerbations with respiratory failure, a number of physicians and a physician organization have recommended that ECMO be considered for persistently high ventilator pressures, uncontrolled respiratory acidosis, or hemodynamic instability. Since our patient qualified for ECMO based on all three suggested criteria, we consulted cardiac surgery for ECMO based on all three suggested instability. Since our patient qualified for respiratory acidosis, or hemodynamic organization have recommended that exacerbations with respiratory failure, with an absolute risk reduction (ARR) of 1–49 days. Hospital mortality was 14.6% in the ECMO group versus 26.2% in the no ECMO group, which equated to an 11.6% absolute risk reduction (P = 0.03) and 52% relative risk reduction (P = 0.04) in mortality. ECMO was associated with hospital costs that were $114,000 higher per patient, compared to the no ECMO group, but did not affect intensive care unit length of stay, hospital length of stay, or time on invasive mechanical ventilation.

We were pleased that our patient had a good outcome, and were reassured by our study results. But we were left to wonder whether ECMO really was the best salvage therapy.
PAST PRESIDENT continued from previous page

opportunities to our members than existed previously and created a home for many different specialists among our membership. We have heard from some of you that the elimination of certain networks led you to feel that CHEST did not adequately value your areas of professional focus. And while we hear you and are working to develop new mechanisms for networking at the annual meeting and throughout the year, the addition of our new sections also allows us to highlight disease states and content domains that previously did not have a clear home in our prior Network structure. CHEST is still learning how to best include and engage groups who have been historically disenfranchised, for whom we want to create new opportunities. The 2021 CHEST President Dr. Steve Simpson identified this as a priority for his presidential year, and we have made strides in the area of diversity, equity, and inclusion.

We launched the First 5 Minutes’ initiative to help clinicians build trust with their patients earlier and more effectively. And CHEST hired the organization’s first Director of Diversity, Equity, Inclusion, and Belonging (DEIB), who has already built our first Value-Setting Work Group and started incorporating DEIB principles into our organizational decision-making. Naively, as we began the year, I was hoping we would make more progress in 2022 than we did. The old dreams were good dreams; they didn’t work out, but I’m glad I had them.

So although there is a great deal more work to do, I know that this is a priority for President Addrizzo-Harris in 2023, and we will continue this positive momentum in the months and years to come. I will retire now to my couch of perpetual indulgence. Yes, I’ve still got the rest of 2023 as an active member of the Board. And, while it has been a great experience, I am looking forward a bit to winding down and letting the fresh faces guide the future of this wonderful organization. Of course, I couldn’t go out without another contest (with an opportunity to win free registration to CHEST 2023!). Five of the sentences in this document come directly from movies; identify the five different movie titles alone are sufficient) and email them to us at contest@chestnet.org. All correct responses received by May 15, 2023, will be entered into a drawing for the prize. Don’t know if there will be a next time, but ’til then.

David

2023 SIMULATION COURSES
CHEST Global Headquarters | Glenview, IL

Introducing new open access journals to the journal CHEST® portfolio

CHEST® Pulmonary and CHEST® Critical Care editors are seeking high-quality submissions in all clinically relevant areas.

Reasons to publish in CHEST Pulmonary and CHEST Critical Care
QUALITY
Brought to you in the same portfolio as the journal CHEST® (11.393 Impact Factor).

HIGH USAGE AND VISIBILITY
Your article will be featured on multiple hosting platforms, including ScienceDirect, which has an audience of more than 1.5 million visitors daily.

OPEN ACCESS
CHEST Pulmonary and CHEST Critical Care are peer-reviewed gold open access journals. Upon acceptance, your article will be available online within days, and it will be permanently and freely available online to read and share.

This month in the journal CHEST®
Editor’s picks

BY PETER J. MAZZONE, MD, MPH, FCCP
Editor in Chief

Guillaume L. Martin, MD, et al.

Evaluation of Dyspnea and Exercise Intolerance After Acute Pulmonary Embolism.
Timothy A. Morris, MD, FCCP, et al.

Tranexamic Acid vs Adrenaline for Controlling Iatrogenic Bleeding During Flexible Bronchoscopy: A Double-Blind Randomized Controlled Trial.
Sonja Badovinac, MD, PhD, et al.

Multidisciplinary ICU Recovery Clinic Visits: A Qualitative Analysis of Patient-Provider Dialogues.
Leanne M. Boehm, PhD, RN, ACNS-BC, et al.

How to Create a Primary Respiratory Care Model.
Russell A. Acevedo, MD, et al.

This month in the journal CHEST®

Editor’s picks

BY PETER J. MAZZONE, MD, MPH, FCCP
Editor in Chief

Keep your knowledge and skill set up to date with our expert-led continuing medical education courses. Get all the relevant updates, plus the irreplaceable benefits of hands-on instruction and practice.

See the Schedule

Learn More & Submit

Learn More & Submit
Next stop, Hawai‘i: A look into the Scientific Program Committee Meeting

Planning for the CHEST Annual Meeting is no small undertaking and begins shortly after the past year’s conference concludes – if not even earlier. Each year, the members of the Scientific Program Committee are tasked with receiving hundreds of submissions and selecting the most clinically compelling ideas to build a meeting program that is both broad in scope, yet also tailored to each specific area of pulmonary, critical care, and sleep medicine.

In mid-February, the CHEST 2023 program began to take shape as the members of the committee met at CHEST Headquarters in Glenview, Illinois, to critically review each and every session. By the end of the 2-day meeting, barring last minute changes, the program was all but completed, and Hawai‘i began to feel very close.

Scenic images of the destination were projected onto the walls, and the room was brimming with excitement for a CHEST meeting unlike any other. Chair of the CHEST Annual Meeting 2023, Aneesa Das, MD, FCCP, focused heavily on the educational experience the meeting will offer while also embracing the culture of Hawai‘i. With two representatives from the state, CHEST 2023 looks to respectfully incorporate Hawaiian customs at every opportunity to supplement the education.

Chair of the Interstitial Lung Disease and Transplant curriculum, Debbie Levine, MD, MS, FCCP, shared that, at least for her section, it was likely the irresistible destination that contributed to the submissions. “Because this meeting is in Hawai‘i, we received the most submissions our group has ever seen,” said Dr. Levine. “And these submissions were top notch – we had really excellent topics to pick from, so this is going to be our best curriculum yet. This is likely true for the other groups, too, so anyone who goes to CHEST 2023 in Hawai‘i will get the best of the best in the most beautiful place in the world.”

With something for everyone in chest medicine, the CHEST 2023 meeting will feature hundreds of sessions covering eight curriculum groups

**Breadth of coverage**

With something for everyone in chest medicine, the CHEST 2023 meeting will feature hundreds of sessions covering eight curriculum groups:

- Critical Care
- Interdisciplinary/Practice Operations/ Education
- Cardiovascular/Pulmonary Vascular Disease
- Intestinal Lung Disease/Transplant
- Lung Cancer/Interventional Pulmonary/ Radiology
- Chest Infections/Disaster Medicine/Systemic Disease

CheST 2023 continued on following page

### The essential care team

As you may have seen in the February issue, in my year as serving President of the American College of Chest Physicians, I will be periodically contributing to CHEST Physician with the latest updates and to serve as a touchpoint for what we are currently working on.

For this contribution, I want to share and reflect upon the recent Nurse Work Environment study published by the American Association of Critical-Care Nurses (AACN). Deployed in 2021, the now-published study concluded that there is serious need for “bold, intentional, and relentless” efforts to create and sustain healthy work environments that foster excellence in patient care and optimal outcomes for patients, nurses, and other members of the health care team.

To achieve this, AACN recommends adhering to the Healthy Work Environments (HWE) Standards created in 2005 but that are more pertinent than ever in 2023. As close partners of the AACN through the Critical Care Societies Collaborative, the CHEST organization applauds and vehemently supports the need for increased efforts to support nurses and other members of the care team.

In a previous article for CHEST Physician, I spoke about my goals for 2023 and one of those goals was to focus on increasing the membership of a variety of providers who help care for patients, including advanced practice providers, respiratory therapists, registered nurses, and others. CHEST is already an inclusive organization to a variety of health care providers, but we can do more, and this is a great time to reemphasize the importance of the care team by showing our support of the AACN and the working conditions of nurses.

Beyond supporting other organizations, the CHEST Board of Regents will focus on new ways to make the organization a valuable resource to every member at every level of their career and with every designation.

The (HWE) Standards that I encourage all CHEST members to support include:

- Skilled communication and true collaboration between doctors, nurses and other clinicians.
- Effective decision-making that includes nurses in the process for input and expertise.
- Appropriate staffing that ensures an effective match between patient needs and the skills of the nurse.
- Meaningful recognition by rewarding and appreciating the value that everyone brings to the team.
- Authentic leadership that embraces a healthy work environment and is supportive of every member of the care team.

Let’s all make a dedicated effort to be intentional in our support of our care team colleagues to improve the working environment and overall patient care.

Think of one thing you can do at your own institution or in your practice to improve the work environment for all those on your team. And then make it happen! Please reach out with ideas or questions.

Doreen J. Addrizzo-Harris, MD, FCCP
Exploring and improving the work environment for nurses

BY CORINNE YOUNG, MSN, FNP-C, FCCP
CHEST Physician Editorial Board Member

If you’ve worked in the ICU then you’ve worked with nurses and, if you’re lucky, you’ve worked with some great ones. Working in multiple units, you may have noticed some differences unit to unit in the dynamics of efficiency, staff retention, and interprofessional dynamics among nurses. Or as the kids would say nowadays, the “vibe” of the unit. The American Association of Critical-Care Nurses (AACN) has been studying the Nurse Work Environment since 2005 with the goal of promoting and improving a Healthy Work Environment (HWE). There are six standards for an HWE according to the AACN, which include: Skilled Communication, True Collaboration, Effective Decision Making, Appropriate Staffing, Meaningful Recognition, and Authentic Leadership. Other than happy nurses, why is an HWE important? Multiple studies have supported that HWEs are associated with high patient satisfaction scores, shorter hospitalization time, increased patient safety, and reduction in adverse events and mortality. Hospitals that get this right can earn the Beacon Award of Excellence, which recognizes units that meet the practices of HWE.

In October 2022, the AACN released its 2021 Nurse Work Environments Status Report earlier than planned to assess how the public health crisis associated with COVID-19 has affected nurses and their work environment. Unsurprisingly, the results were dissatisfactory; 9,335 nurses from 50 states participated. Starting with the worse score, appropriate staffing, only 20% reported having appropriate and skilled staffing at least 75% of the time in 2021. That is the lowest recorded report, even lower than it was during the 2006 nursing shortage. Less than 50% felt their organization valued their health and safety, and 72% stated they were verbally, physically, or sexually assaulted on the job. In regard to quality, only 30% of nurses felt the quality of care in their unit was excellent; however, nurse managers, being the optimists that they are, reported higher at 41%. Satisfaction took a nosedive especially in units where HWEs were not implemented. Only 34% of these nurses felt satisfied with their job, and 67% intend on leaving their employer in the next 3 years. Thirty percent of nurses would recommend their unit, and 20% would recommend their employer to others. During the last survey in 2018, 62% of nurses were very satisfied with being a nurse, but, sadly, this dropped to 40% in 2021. Of note, Beacon units did perform higher in most reported areas despite the hardships of COVID-19.

Nurses are the foundation supporting our plan of care, patient outcomes, and patient advocacy. Improving the nurse work environment benefits the entire care team and, most importantly, patient outcomes. Improving the nurse work environment benefits the entire care team and, most importantly, patient outcomes. Improving the nurse work environment benefits the entire care team and, most importantly, patient outcomes. AACN recommendations to promote an HWE would require systems to create environments where work is respected and honored, improve communication where a nursing voice is heard in regard to patient care decision making, provide staffing levels that are both appropriate and skilled, and ensure nurses feel valued. As part of the care team, we can hear our nurses and advocate for them. We can have conversations with administration regarding creating HWEs and striving for Beacon status. We can engage nurses in policy development that affects their unit. And, we can stop showing nurses how valuable they are with pizza and give them more meaningful feedback instead. In the 2021 survey, nurses reported positive feedback from patients and families was more meaningful to them than free meals. Encourage your patients and families to give that needed feedback. We could all be better stewards of the nursing profession and starting a conversation about HWEs is a great place to start.
OCT budesonide-formoterol could save lives, money

BY ESTHER LANDHUIS

I

It budesonide-formoterol were to become available over the counter (OTC) and used as-needed for mild asthma, it would save lives and cut health care costs, according to a computer modeling study presented at the American Academy of Allergy, Asthma, and Immunology 2023 annual meeting in San Antonio.

Asthma affects 25 million people, about 1 in 13, in the United States. About 28% are uninsured or underinsured, and 70% have mild asthma. Many are using a $30 inhaled epinephrine product (Primatene Mist) — the only FDA-approved asthma inhaler available without a prescription, said Marcus Shaker, MD, MS, professor of pediatrics and medicine at Geisel School of Medicine at Dartmouth, and clinician at Dartmouth Health Children’s, N.H.

A new version of Primatene Mist was reintroduced on the market in 2018 after the product was pulled for containing chlorofluorocarbons in 2011, but it is not recommended by professional medical societies because of safety concerns over epinephrine’s adverse effects, such as increased heart rate and blood pressure.

Drugs in its class (bronchodilators) have long been associated with a higher risk for death or near-death.

Meanwhile, research more than 2 decades ago linked regular use of low-dose inhaled corticosteroids with reduced risk for asthma death.

More recently, two large studies (SYGMA 1 and SYGMA 2) compared maintenance therapy with a low-dose inhaled corticosteroid (budesonide) vs. on-demand treatment with an inhaler containing both a corticosteroid (budesonide) and a long-acting bronchodilator (formoterol).

"Using as-needed budesonide-formoterol led to outcomes that are almost as good as taking a maintenance budesonide dose every day," said Dr. Shaker, who presented the results at an AAAAI oral abstract session.

The cost savings emerged even though in the United States asthma controller therapies (for example, fluticasone) cost about 10 times more than rescue therapies (for instance, salbutamol, OTC epinephrine).

Nevertheless, the results make sense. "If you’re using Primatene Mist, your health costs are predicted to be much greater because you’re going to be in the hospital more. Your asthma is not going to be well-controlled," Thanai Pongdee, MD, an allergist-immunologist with the Mayo Clinic in Rochester, Minn., told this news organization. "It’s not only the cost of your ER visit but also the cost of loss of work or school, and loss of daily productivity. There are all these associated costs."

The analysis "is certainly something policy makers could take a look at," he said.

He noted that current use of budesonide-formoterol is stymied by difficulties with insurance coverage. The difficulties stem from a mismatch between the updated recommendation for as-needed use and the description printed on the brand-name product (Symbicort).

"On the product label, it says Symbicort should be used on a daily basis," Dr. Pongdee said. "But if a prescription comes through and says you’re going to use this ‘as needed,’ the health plan may say that’s not appropriate because that’s not on the product label.”

Given these access challenges with the all-in-one inhaler, other researchers have developed a workaround — asking patients to continue their usual care (that is, using a rescue inhaler as needed) but to also administer a controller medication after each rescue. When tested in Black and Latino patients with moderate to severe asthma, this easy strategy (patient activated reliever-triggered inhaled corticosteroid, or PARTICS) reduced severe asthma exacerbations about as well as the all-in-one inhaler.

If the all-in-one budesonide-formoterol does become available OTC, Dr. Shaker stressed that it "would not be a substitute for seeing an allergist and getting appropriate medical care and an evaluation and all the rest. But it’s better than the status quo. It’s the sort of thing where the perfect is not the enemy of the good," he said.

Dr. Shaker is the AAAAI cochair of the Joint Task Force on Practice Parameters and serves as an editorial board member of the Journal of Allergy and Clinical Immunology in Practice. He is also an associate editor of the Annals of Allergy, Asthma, and Immunology.

Dr. Pongdee serves as an at-large director on the AAAAI board of directors. He receives grant funding from GlaxoSmithKline, and Mayo Clinic is a trial site for GlaxoSmithKline and AstraZeneca.
Sputum markers may predict remission in eosinophilic asthma

BY HEIDI SPLETE
MEDedge News

Specific sputum markers, including higher sputum eosinophils, macrophages, and lymphocyte counts, were associated with remission after interleukin-5 (IL-5)–targeted therapy for patients with severe eosinophilic asthma. The finding was based on data from 52 individuals. Although IL-5 therapies have been shown to be effective for improving asthma, patients’ responses vary, write Catherine Moermans, PhD, of Liège University, Belgium, and colleagues. Biotherapies targeting IL-5 allow a tangible improvement in the sputum of each patient.

In an observational study published in the journal Chest (2023. doi: 10.1016/j.chest.2023.01.037), the researchers recruited 52 adults with severe asthma who began anti–IL-5 treatment at a single center. The primary outcome was asthma remission. Remission was defined as meeting all of the following criteria 1 year after therapy: no chronic treatment with oral corticosteroids; no exacerbation; asthma control questionnaire scores lower than 1.5 and/or asthma test greater than 19; forced expiratory volume in 1 second (FEV1) of at least 80% predicted; and/or improvement of FEV1 equal to or larger than 10%, and a blood eosinophil count lower than 300 cells/mL.

Prior to treatment, the researchers measured eosinophil peroxidase (EPX), immunoglobulin E (IgE), IL-3, IL-4, IL-5, IL-13, IL-25, IL-33, granulocyte-macrophage colony-stimulating factor (GM-CSF), thymic stromal lymphopoietin (TSLP), and eotaxin-1 levels in the sputum of each patient. At follow-up, 11 patients met the criteria for remission. These patients had significantly higher sputum eosinophil counts, sputum macrophage counts, and lymphocyte counts at baseline, compared with those not in remission (P = .006, P = .02, and P = .04, respectively). Sputum neutrophil percentage levels were significantly lower in patients whose asthma was in remission, compared with those whose asthma was not in remission (P = .007).

At the protein level, remission patients also showed higher baseline levels of sputum eotaxin-1, TSLP, IL-5, EPX, and IgE protein, compared with patients who did not achieve remission (P = .046, P = .04, P = .002, P = .001, and P = .006, respectively).

Overall, EPX and IL-5 measures showed the best combination of sensitivity and specificity, as well as the best area under the curve, the researchers write.

Patients in remission were significantly more likely to be men (8 of 11 patients), a finding that reflected previous studies, the researchers write. The finding of eosinophilic inflammation associated with stronger response to anti–IL-5 therapy also reflected previous studies, but the current study showed that, “with a comparable blood eosinophil level at baseline before biotherapy, the response can be highly variable.”

The study findings were limited by several factors, including small sample size and no formal definition of remission. Other research needs include an analysis based on non-response or suboptimal response predictors. Results suggest that sputum type 2 markers are potential predictors of remission after anti–IL-5 treatment in adults with severe eosinophilic asthma, although they must be validated in a larger, multicenter cohort, they concluded.

The study was supported by GlaxoSmithKline and AstraZeneca. Several coauthors have relationships with these companies. Dr. Moermans had no relevant conflicts.

Irregular sleep – such as inconsistent sleep duration or sleep timing – may increase the risk of developing atherosclerosis among adults older than age 45, a new report suggests.

In particular, variation in sleep duration of more than 2 hours per night in the same week was tied to higher rates of atherosclerosis.

“Poor sleep is linked with several cardiovascular conditions, including heart disease, hypertension, and type 2 diabetes,” lead author Kelsie M. Full, PhD, MPH, assistant professor of medicine at Vanderbilt University Medical Center, Nashville, Tenn., said in an interview.

“Overall, we found that participants who slept varying amounts of hours throughout the week (meaning that one night they slept less, one night they slept more) were more likely to have atherosclerosis than participants who slept about the same amount of time each night,” she said.

The study was published online in the Journal of the American Heart Association (2023 Feb 15. doi: 10.1161/JAHA.122.027361).

**Analyzing associations**

Dr. Full and colleagues examined data from 2,032 participants in the Multi-Ethnic Study of Atherosclerosis Sleep Ancillary Study, which included adults aged between 45 and 84 years in six U.S. communities who completed 7-day wrist actigraphy assessment and kept a sleep diary between 2010 and 2013.

For subclinical markers of cardiovascular disease, participants underwent assessments of coronary artery calcium, carotid plaque presence, carotid intima-media thickness, and ankle-brachial index.

The research team assessed sleep duration, or the total number of minutes of sleep in a night, and sleep timing regularity, which was determined on the basis of the time someone initially fell asleep each night. They adjusted for cardiovascular disease risk factors and sleep characteristics, such as obstructive sleep apnea, sleep duration, and sleep fragmentation.

The average age of the participants was 68.6 years, and 53.6% were women. About 37.9% identified as White, 27.6% as Black or African American, 23.4% as Hispanic American, and 11.1% as Chinese American.

During the 7-day period, about 38% of participants experienced a change in sleep duration of more than 90 minutes, and 18% experienced a sleep duration change of more than 120 minutes. Those who had irregular sleep were more likely to be non-White, current smokers, have lower average annual incomes, have work shift schedules or did not work, and have a higher average body mass index.

For the study, sleep duration irregularity was defined as a standard deviation of more than 120 minutes.

Those participants who had a greater degree of sleep irregularity were more likely to have high coronary artery calcium burden than those whose sleep duration was more regular, defined as an SD of 60 minutes or less (< 300; prevalence ratio, 1.33; 95% confidence interval, 1.03-1.71), as well as abnormal ankle-brachial index (< 0.9; prevalence ratio, 1.75; 95% CI, 1.03-2.95).

Further, those with irregular sleep timing (SD > 90 minutes) were more likely to have a high coronary artery calcium burden (prevalence ratio, 1.39; 95% CI, 1.07-1.82) in comparison with those with more regular sleep timing (SD < 30 minutes).

“The biggest surprise to me was that 30% of the participants in the study had total sleep times that varied by more than 90 minutes over the course of the week,” Dr. Full said. “This is consistent with prior studies that suggest that a large proportion of the general public have irregular sleep patterns, not just shift workers.”

In additional analyses, Dr. Full and colleagues found that sleep duration regularity continued to be associated with high coronary artery calcium burden and abnormal ankle-brachial index accounting for severe obstructive sleep apnea, average nightly sleep duration, and average sleep fragmentation.

Notably, when sleep duration was added, all participants with more irregular sleep durations (SD > 60 minutes) were more likely to have a high coronary artery calcium burden, compared with those with regular sleep durations (SD < 60 minutes). The results remained when participants who reported shift work, including night-shift work, were excluded.

Additional studies are needed to understand the mechanisms, the study authors wrote. Night-to-night variability in sleep duration and sleep timing can cause desynchronization in the sleep-wake timing and circadian disruption.

“A key issue highlighted in this study is that sleep irregularity itself, independent of how much sleep people were getting, was related to heart health. Sleep is a naturally occurring phenomenon, and maintaining regularity helps provide stability and predictability to the body,” Michael Grandner, PhD, associate professor of psychiatry and director of the sleep and health research program at the University of Arizona, Tucson, said in an interview.

Dr. Grandner, who wasn’t involved with this study, has researched sleep irregularity and associations with cardiovascular disease, diabetes, obesity, and many other adverse outcomes.

“When people have very irregular sleep schedules, it may make it harder for the body to optimally make good use of the sleep it is getting, since it such a moving target,” he said. “The unique angle here is the ability to focus on regularity of sleep.”

The study was supported by the National Heart, Lung, and Blood Institute and the National Center for Advancing Translational Sciences of the National Institutes of Health. One author received grants and consulting fees from pharmaceutical companies unrelated to the research. The other authors and Dr. Grandner disclosed no relevant financial relationships.

**ILD continued from previous page**

of patients with preclinical or subclinical ILD and clinical ILD, the commentary authors write. “It is therefore conceivable that some patients with rheumatoid arthritis diagnosed with preclinical or subclinical ILD could potentially have worse outcomes if both the rheumatoid arthritis and ILD are not monitored closely,” they noted.

To better track RA-associated ILD for patients with and those without symptoms, the authors advocate for monitoring patients using pulmonary testing and CT scanning, as well as evaluating symptoms. How often these assessments should be conducted depends on the individual, they note. In her own practice, Dr. Volkman sees patients every 3 months to evaluate their symptoms and conduct pulmonary function tests (PFTs). For patients early in the course of ILD, she orders HRCT imaging once per year.

For Dr. Davis, the frequency of follow-up depends on the severity of ILD. “For minimally symptomatic patients without compromised lung function, we would generally follow annually. For patients with symptomatic ILD on stable therapy, we may monitor every 6 months. For patients with active/progressive ILD, we would generally be following at least every 1-3 months,” he said.

**Screening and future research**

While there is no evidence to recommend screening patients for ILD using CT, there are certain risk factors for ILD in RA patients, including a history of smoking, male sex, and high RA disease activity despite antirheumatic treatment, Dr. Volkman said. In both of their practices, Dr. Davis and Dr. Volkman screen with CT and PFTs for ILD for patients with known risk factors that predispose them to the lung condition and/or for patients who report respiratory symptoms.

“We still don’t have an algorithm [for screening patients], and that is a desperate need in this field,” added Joshua J. Solomon, MD, a pulmonologist at National Jewish Health, Denver, whose research focuses on RA-associated ILD. While recommendations state that all patients with scleroderma should be screened with CT, ILD incidence is lower among patients with RA, and thus these screening recommendations need to be narrowed, he said. But more research is needed to better fine-tune recommendations, he said. “The only thing you can do is give some expert consensus until there are good data.”

Dr. Volkman has received consulting and speaking fees from Boehringer Ingelheim and institutional support for performing studies on systemic sclerosis for Kadmon, Forbius, Boehringer Ingelheim, Horizon, and Prometheus. Dr. Gordon, Dr. Davis, and Dr. Solomon report no relevant financial relationships.
Pulmonary function may predict frailty

BY HEIDI SPLETE

Pulmonary function was significantly associated with frailty in community-dwelling older adults over a 5-year period, as indicated by data from more than 1,000 individuals.

The pulmonary function test has been proposed as a predictive tool for clinical outcomes in geriatrics, including hospitalization, mortality, and frailty, but data on the relationship between pulmonary function and frailty in community-dwelling adults are limited and inconsistent, write Walter Sepulveda-Loyola, MD, of Universidad de Las Americas, Santiago, Chile, and colleagues.

In an observational study published in Heart and Lung (2023 Feb 14. doi: 10.1016/j.hrtlng.2023.01.020), the researchers reviewed data from adults older than 64 years who were participants in the Toledo Study for Healthy Aging.

The study population included 1,188 older adults (mean age, 74 years; 54% women). The prevalence of frailty at baseline ranged from 7% to 26%.

Frailty was defined using the frailty phenotype (FP) and the Frailty Trait Scale 5 (FTS5). Pulmonary function was determined on the basis of forced expiratory volume in the first second (FEV₁) and forced vital capacity (FVC), using spirometry.

Overall, at the 5-year follow-up, FEV₁ and FVC were inversely associated with prevalence and incidence of frailty in nonadjusted and adjusted models using FP and FTS5.

In adjusted models, FEV₁ and FVC, as well as FEV₁ and FVC percent predicted value, were significantly associated with the prevalence of frailty.

In adjusted models, FEV₁ and FVC, as well as FEV₁ and FVC percent predicted value, were significantly associated with the prevalence of frailty.

In adjusted models, FEV₁ and FVC, as well as FEV₁ and FVC percent predicted value, were significantly associated with the prevalence of frailty.

In adjusted models, FEV₁ and FVC, as well as FEV₁ and FVC percent predicted value, were significantly associated with the prevalence of frailty.

In adjusted models, FEV₁ and FVC, as well as FEV₁ and FVC percent predicted value, were significantly associated with the prevalence of frailty.

In adjusted models, FEV₁ and FVC, as well as FEV₁ and FVC percent predicted value, were significantly associated with the prevalence of frailty.

Pulmonary function also was associated with prevalent and incident frailty, hospitalization, and mortality in regression models, including the whole sample and after respiratory diseases were excluded.

Pulmonary function measures below the cutoff points for FEV₁ and FVC were significantly associated with frailty, as well as with hospitalization and mortality. The cutoff points for FEV₁ were 1.805 L for men and 1.165 L for women; cutoff points for FVC were 2.385 L for men and 1.585 L for women. “Pulmonary function should be evaluated not only in frail patients, with the aim of detecting patients with poor prognoses regardless of their comorbidity, but also in individuals who are not frail but have an increased risk of developing frailty, as well as other adverse events,” the researchers write.

The study findings were limited by lack of data on pulmonary function variables outside of spirometry and by the need for data from populations with different characteristics to assess whether the same cutoff points are predictive of frailty, the researchers note.

The results were strengthened by the large sample size and additional analysis that excluded other respiratory diseases. Future research should consider adding pulmonary function assessment to the frailty model, the authors write.

Given the relationship between pulmonary function and physical capacity, the current study supports more frequent evaluation of pulmonary function in clinical practice for older adults, including those with no pulmonary disease, they conclude.

The study was supported by the Spanish Ministry of Economy, Industry, and Competitiveness, financed by the European Regional Development Funds, and the Centro de Investigacion Biomédica en Red en Envejecimiento y Envejecimiento Saludable and the Fundacion Francisco Soria Melguizo. Lead author Dr. Sepulveda-Loyola was supported by the Brazilian National Council for Scientific and Technological Development.
Eight-week TB treatment strategy shows promise

BY NANCY A. MELVILLE

A strategy for the treatment of tuberculosis involving just an 8-week treatment regimen—along with close posttreatment monitoring and treatment extension if needed—shows potential as an effective alternative to the standard 24-week regimen.

“We found that if we use the strategy of a bedaquiline-linezolid five-drug regimen for 8 weeks and then followed patients for 96 weeks, [the regimen] was noninferior, clinically, to the standard regimen in terms of the number of people alive, free of TB disease, and not on treatment,” said lead author Nicholas Paton, MD, of the National University of Singapore, in a press conference held during the Conference on Retroviruses & Opportunistic Infections.

“The total time on treatment was reduced by half—instead of 160 days, it was 85 days for the total duration.”

Commenting on the study, which was published concurrently in the New England Journal of Medicine (2023 Feb 20. doi: 10.1056/NEJMoa2212537), Richard E. Chaisson, MD, noted that, although more needs to be understood, the high number of responses is nevertheless encouraging.

“Clinicians will not feel comfortable with the short regimens at this point, but it is remarkable that so many patients did well with shorter treatments,” Dr. Chaisson, who is a professor of medicine, epidemiology, and international health and director of the Johns Hopkins University Center for Tuberculosis Research, Baltimore, said in an interview.

Importantly, the study should help push forward “future studies [that] will stratify patients according to their likelihood of responding to shorter treatments,” he said.

The current global standard for TB treatment, practiced for 4 decades, has been a 6-month rifampin-based regimen. Although this regimen performs well, curing more than 95% of cases in clinical trials, in real-world practice, the prolonged duration can be problematic, with issues of nonadherence and loss of patients to follow-up.

Previous research has shown that shorter regimens have potential, with some studies showing as many as 85% of patients cured with 3- and 4-month regimens, and some promising 2-month regimens showing efficacy specifically for those with smear-negative TB.

These efforts suggest that “the current 6-month regimen may lead to overtreatment in the majority of persons in order to prevent relapse in a minority of persons,” the authors asserted.

TRUNCATE-TB

To investigate a suitable shorter-term alternative, the authors conducted the phase 2-3, prospective, open-label TRUNCATE-TB trial, in which 674 patients with rifampin-susceptible pulmonary TB were enrolled at 18 sites in Asia and Africa.

The patients were randomly assigned to receive either the standard treatment regimen (rifampin and isoniazid for 24 weeks with pyrazinamide and ethambutol for the first 8 weeks; n = 181), or one of four novel five-drug regimens to be administered over 8 weeks, along with extended treatment for persistent clinical disease of up to 12 weeks, if needed, and a plan for retreatment in the case of relapse (n = 493).

Two of the regimens were dropped because of logistic criteria; the two remaining shorter-course groups included in the study involved either high-dose rifampin plus linezolid or bedaquiline plus linezolid, each combined with isoniazid, pyrazinamide, and ethambutol.

Of the patients, 62% were male, and four withdrew or were lost to follow-up by the end of the study at a final follow-up at week 96.

Among patients assigned to the 8-week regimens, 80% stopped at exactly 8 weeks, while 9% wound up having extended treatment to 10 weeks and 3% were extended to 12 weeks.

For the primary endpoint, a composite of death, ongoing treatment, or active disease at week 96, the rate was lowest in the standard 24-week therapy group, occurring in 7 of 181 patients (3.9%), compared with 21 of 184 patients (11.4%) in the rifampin plus linezolid group (adjusted difference, 7.4 percentage points, which did not meet noninferiority criterion), and 11 of 189 (5.8%) in the group in the bedaquiline plus linezolid group (adjusted difference, 0.8 percentage points, meeting noninferiority criterion).

The mean total duration of treatment through week 96 in the standard treatment group was 180 days versus 106 days in the rifampin–linezolid group, and 85 days in the bedaquiline-linezolid group.

The results were consistent across multiple subgroup analyses defined according to baseline characteristics, including some that could be linked to severe disease and a high risk for relapse.

In terms of safety, there were no significant differences between the groups in terms of grade 3 or 4 adverse events.

Of note, only two patients (1.1%) in the bedaquiline plus linezolid group acquired a resistance, which Dr. Paton said was “encouraging,” because of concerns about resistance to that drug.

Dr. Dartois reported no relevant financial relationships. Dr. Chaisson had no disclosures to report.
This advertisement is not available for the digital edition.