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CHEST® Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

Doucefleur/Getty Images

Cardiovascular impact of smoking may last up to 25 years

BY BIANCA NOGRADY
MDedge News

Quitting smoking significantly reduces the risk of cardiovascular disease, but past smokers are still at elevated cardiovascular risk, compared with nonsmokers, for up to 25 years after smoking cessation, research in JAMA suggests.

A retrospective analysis of data from 8,770 individuals in the Framingham Heart Study compared the incidence of myocardial infarction, stroke, heart failure, or cardiovascular death in ever-smokers with that of never-smokers.

Only 40% of the total cohort had never smoked. Of the 4,115 current smokers at baseline, 38.6% quit during the course of the study and did not relapse but 51.4% continued to smoke until they developed cardiovascular disease or dropped out of the study.

Current smokers had a significant 4.68-fold higher incidence of cardiovascular disease, compared with those who had never smoked, but those who stopped smoking showed a 39% decline in their risk of cardiovascular disease within 5 years of cessation.

However, individuals who were formerly heavy smokers – defined as at least 20 pack-years of smoking – retained a risk of cardiovascular disease 25% higher than that of never-smokers until 10-15 years after quitting smoking. At 16

SMOKING // *continued on page 6*

Post-sepsis inflammation biomarkers flag mortality risk

BY JEFF CRAVEN
MDedge News

Inflammation and immunosuppression can persist for some patients up to a year after a hospitalization for sepsis, and these patients are more likely to experience worsened long-term outcomes, readmission after discharge, and mortality, according to a study published in JAMA Network Open.

"Individuals with persistent biomarkers of inflammation and immunosuppression had a higher risk of readmission and death due to cardiovascular disease and cancer compared with those with normal circulating biomarkers," Sachin Yende, MD, of the VA Pittsburgh Healthcare System and the University of Pittsburgh and colleagues wrote. "Our findings suggest that long-term immunomodulation strategies should be explored in patients hospitalized with sepsis."

Dr. Yende and colleagues performed a multicenter, prospective cohort study of 483 patients who were hospitalized for sepsis at 12 different sites between January 2012 and May 2017. They measured inflammation using interleukin-6,

SEPSIS // *continued on page 7*

INSIDE HIGHLIGHT

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FDA takes another swing at cigarette pack warnings

BY M. ALEXANDER OTTO
MDedge News

The U.S. Food and Drug Administration has proposed warnings for cigarette packs and advertisements on Aug. 15, 2019, that feature graphic, colored images illustrating the harms of smoking, but this could be subjected to legal challenge.

Several years ago, tobacco companies filed a law suit, which ultimately shut down a similar proposal.

The warnings focus on lesser-known complications – including diabetes, cataracts, gangrene, stroke, bladder cancer, erectile dysfunction, and obstructive pulmonary disease – and would take up the top half of the front and back of cigarette packs, and at least the top 20% of print advertisements. Each pack and ad would be required to carry 1 of

the 13 proposed warnings, according to the announcement.

The approach would be similar to, but not as aggressive as Canada's. For years, cigarettes packs sold in Canada have included disturbing photographs of diseased lungs, rotted teeth, and dying patients. The lasting impact of such imagery has been demonstrated in the literature (for example, Am J Prev Med. 2007 Mar;32[3]:202-9).

The new proposal is the FDA's second attempt to enact something comparable in the United States, after being directed to do so by the Tobacco Control Act of 2009.

The first effort to add strong, illustrated warnings to cigarette packs was widely backed by medical groups, but challenged in the courts by R.J. Reynolds and other tobacco companies, and blocked on appeal in 2012 as an abridgment of commercial free speech. The federal government dropped the case in 2013.

The American Lung Association and other public health groups subsequently sued the FDA in 2016 to enact the Tobacco Act mandate. A federal judge then ordered the agency to publish a new rule by August 2019, and issue a final rule in March 2020.

This time around, the FDA "took the necessary time to get these new proposed warnings right ... based on – and within the limits of – both science and the law," the agency said. The new images, though graphic, are less disturbing than those used in Canada and the agency's previous proposals, which included an apparent corpse with a sternotomy. The 1-800-Quit-Now cessation hotline number, which was a sticking point in the 2012 ruling, has also been dropped.

U.S. Food and Drug Administration

The proposed warnings would cover half the pack.

When asked about the new efforts, R.J. Reynolds spokesperson Kaelan Hollon said, "We are carefully reviewing FDA's latest proposal for graphic warnings on cigarettes. We firmly support public awareness of the harms of smoking cigarettes, but the manner in which those messages are delivered to the public cannot run afoul of the First Amendment protections that apply to all speakers, including cigarette manufacturers."

Warnings on U.S. cigarettes haven't changed since 1984, when the risks of lung cancer, heart disease, emphysema, and pregnancy complications were added to the side of cigarette packs. With time, the FDA said the surgeon general's warnings have become "virtually invisible" to consumers.

The American Lung Association, American Academy of Pediatrics, and other plaintiffs in the 2016 suit called the new proposal a "dramatic improvement" over the current situation and "long overdue" in a joint statement on Aug. 15.

Although rates have declined substantially in recent decades, about 34.3 million U.S. adults and almost 1.4 million teenagers still smoke.

Comments on the proposed rule are being accepted through Oct. 15. The agency is open to suggestions for alternative text and images.

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Smoking cessation had effect on risk

// continued from page 1

years, the 95% confidence interval for cardiovascular disease risk among former smokers versus that of never-smokers finally and consistently included the null value of 1.

The study pooled two cohorts; the original cohort, who attended their fourth examination during 1954-1958 and an offspring cohort who attended their first examination during 1971-1975. The authors saw a difference between the two cohorts in the time course of cardiovascular disease risk in heavy smokers.

In the original cohort, former heavy smoking ceased to be significantly associated with increased cardiovascular disease risk within 5-10 years of cessation, but in the offspring cohort, it took 25 years after cessation for the incidence to decline to the same level of risk seen in never-smokers.

"The upper estimate of this time course is a decade longer than that of the Nurses' Health Study results for coronary heart disease and cardiovascular death and more than 20 years longer than in some prior reports for coronary heart disease and stroke," wrote Meredith S. Duncan from the division of cardiovascular medicine at the Vanderbilt University Medical Center, Nashville, Tenn., and coauthors. "Although the exact amount of time after quitting at which former smokers' CVD risk ceases to differ significantly from that of never-smokers is unknown (and may further depend on cumulative exposure), these findings support a longer time course of risk reduction than was previously thought, yielding implications for CVD risk stratification of former smokers."

However, they did note that the study could not account for environmental tobacco smoke exposure and that the participants were mostly of white European ancestry, which limited the generalizability of the findings to other populations.

The Framingham Health Study was supported by the National Heart, Lung, and Blood Institute. One author declared a consultancy with a pharmaceutical company on a proposed clinical trial. No other conflicts of interest were declared.

SOURCE: Duncan M et al. JAMA 2019. doi: 10.1001/jama.2019.10298.

Vaping illness cases now over 150, CDC says

BY DENISE FULTON

MDedge News

More than 150 cases of severe lung illness possibly related to e-cigarette use in adolescents and young adults have been reported in 16 states, according to an Aug. 21 update from officials at the Centers for Disease Control and Prevention.

Officials from the CDC and the Food and Drug Administration are working with state health officials to gather information on the cases as well as any products or substances that might be involved.

A total of 153 potential cases were reported between June 28 and Aug. 20 in 16 states – California, Connecticut, Florida, Illinois, Indiana, Iowa, Michigan, Minnesota, New Jersey, New Mexico, New York, North Carolina, Pennsylvania, Texas, Utah, and Wisconsin.

Health officials have yet to find a cause for these illnesses; however, all patients have reported e-cigarette use or vaping, according to a CDC statement. Evidence to date does not seem to indicate that an infectious agent is the cause.

In general, patients have reported a gradual onset of symptoms including shortness of breath and/or chest pain that increased over days or weeks before hospital admission. Gastrointestinal symptoms including vomiting, diarrhea, and fatigue have been reported by some.

Many patients reported using products containing tetrahydrocannabinol, though no specific or consistent product has been linked definitively.

While cases reported across the country seem to be similar, there is no evidence currently indicating they have a common cause, according to the CDC statement.

The CDC is urging health care professionals to report possible cases to their state or local health department and the FDA is urging the public to provide detailed reports of any unusual or unexpected health concerns related to tobacco use or e-cigarette use through its Safety Reporting Portal.

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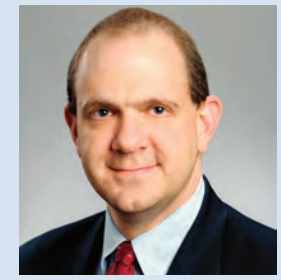

David A. Schulman, MD, FCCP, is Medical Editor in Chief of *CHEST Physician*.

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Immunosuppression in sepsis survivors linked to 6-month readmission

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high-sensitivity C-reactive protein (hs-CRP), and soluble programmed death-ligand 1 (sPD-L1); hemostasis using plasminogen activator inhibitor 1 and D-dimer; and endothelial dysfunction using intercellular adhesion molecule 1, vascular cell adhesion molecule 1, and E-selectin. The patients included were mean age 60.5 years, 54.9% were male, the mean Sequential Organ Failure Assessment score was 4.2, and a total of 376 patients (77.8%) had one or more chronic diseases.

Dr. Yende

Overall, there were 485 readmissions in 205 patients (42.5%). The mortality rate was 43 patients (8.9%) at 3 months, 56 patients (11.6%) at 6 months, and 85 patients (17.6%) at 12 months. At 3 months, 23 patients (25.8%) had elevated hs-CRP levels, which increased to 26 patients (30.2%) at 6 months and 40 patients (44.9%) at 12 months. sPD-L1 levels were elevated in 45 patients (46.4%) at 3 months, but the number of patients with elevated sPD-L1 did not appear to significantly increase at 6 months (40 patients; 44.9%) or 12 months (44 patients; 49.4%).

Researchers developed a phenotype of hyperinflammation and immunosuppression that consisted of 326 of 477 (68.3%) patients with high hs-CRP and elevated sPD-L1 levels. Patients with this phenotype of hyperinflammation and immunosuppression had more than 8 times the risk of 1-year mortality (odds ratio, 8.26; 95% confidence interval, 3.45-21.69; *P* less than .001) and more than 5 times the risk of readmission or mortality at 6 months related to cardiovascular disease (hazard ratio, 5.07; 95% CI, 1.18-21.84; *P* = .02) or cancer (hazard ratio, 5.15; 95% CI, 1.25-21.18; *P* = .02), compared with patients who had normal hs-CRP and sPD-L1 levels. This hyperinflammation and immunosuppression phenotype also was associated with greater risk of 6-month all-cause readmission or mortality (HR, 1.53; 95% CI, 1.10-2.13; *P* = .01), compared with patients who had the normal phenotype.

"The persistence of hyperinflammation in a large number of sepsis survivors and the increased risk of cardiovascular events among these patients may explain the association between infection and cardiovascular disease in a prior study," the authors said. "Although prior trials tested immunomodulation strategies during only the early phase of hospitalization for sepsis, immunomodulation may be needed after hospital discharge," and the findings of this trial suggest points of future study for patients who survive sepsis and develop long-term sequelae.

This study was funded by grants from National Institutes of Health and resources from the VA Pittsburgh Healthcare System. The authors reported personal and institutional relationships in the form of personal fees, grants, and patents for Alung Technologies, Atox Bio, Bayer AG, Beckman Coulter, BristolMyers Squibb, Ferring, NIH, Roche, Selepressin, and the University of Pittsburgh.

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SOURCE: Yende S et al. JAMA Netw Open. 2019 Aug 7. doi: 10.1001/jamanetworkopen.2019.8686.

VIEW ON THE NEWS

Eric J. Gartman, MD, FCCP, comments:

The longevity of debility in survivors of critical illness and sepsis clearly extends beyond the hospital stay – whether in the form of impaired functionality, cognitive decline, or abnormalities in immune and inflammatory responses as described in this research. This study's data demonstrating long-term persistent changes in inflammation and immune function in a large subset of sepsis survivors are concerning, as these changes may be responsible for a high level of subsequent morbidity and mortality. It is unclear if there are pre-existing patient-level factors leading to the initial sepsis event that may ultimately be responsible for the long-term inflammatory profile of the patient and, thus, may not be modifiable (e.g., underlying malignancy, dementia, advanced medical disease, etc.). However, given the associations that were shown, this certainly warrants further investigation.

Global study outlines effect of climate change on health

BY TARA HAELLE

MDedge News

Regardless of where people live in the world, air pollution is linked to increased rates of cardiovascular disease, respiratory problems, and all-cause mortality, according to one of the largest studies ever to assess the effects of inhalable particulate matter (PM), published in the New England Journal of Medicine.

"These data reinforce the evidence of a link effect between mortality and PM concentration established in regional and local studies," reported Cong Liu of the Huazhong University of Science and Technology in Wuhan, China, and an international team of researchers.

"Many people are experiencing worse allergy and asthma symptoms in the setting of increased heat and worse air quality," Caren G. Solomon, MD, of Harvard Medical School, Boston, said in an interview. "It is often not appreciated that these are complications of climate change."

Other such complications include heat-related illnesses and severe weather events, as well as the less visible manifestations, such as shifts in the epidemiology of vector-borne infectious disease, Dr. Solomon and colleagues wrote in an editorial accompanying Mr. Liu's study.

"The stark reality is that high levels of greenhouse gases caused by the combustion of fossil fuels – and the resulting rise in temperature and sea levels and intensification of extreme weather – are having profound consequences for human health and health systems," Dr. Solomon and colleagues wrote (N Engl J Med. 2019;381:773-4.).

Mr. Liu and colleagues analyzed 59.6 million deaths from 652 cities across 24 countries, "thereby greatly increasing the generalizability of the association and decreasing the likelihood that the reported associations are subject to confounding bias," wrote John R. Balmes, MD, of the University of California, San Francisco, and the University of California, Berkeley, in an editorial about the study (N Engl J Med. 2019;381:774-6).

The researchers compared air pollution data from 1986-2015 from the Multi-City Multi-Country (MCC) Collaborative Research Network to mortality data reported from individual countries. They assessed PM with an aerodynamic diameter of 10 mcg or less (PM_{10}; n = 598 cities) and PM with an aerodynamic diameter of 2.5 mcg or less ($PM_{2.5}$; n = 499 cities).

Mr. Liu's team used a time-series analysis – a standard upon which the majority of air pollution research relies. These studies "include daily measures of health events (e.g., daily mortality), regressed against concentrations of PM (e.g., 24-hour average $PM_{2.5}$) and weather variables (e.g., daily average temperature) for a given geographic area," Dr. Balmes wrote. The researchers found a 0.44% increase in daily all-cause mortality for each 10-mcg/m^3 increase in the 2-day moving average (current and previous day) of PM_{10}. The same increase was linked to a 0.36% increase in daily cardiovascular mortality and a 0.47% increase in daily respiratory mortality. Similarly, a 10-mcg/m^3 increase in the $PM_{2.5}$ average was linked to a 0.68% increase in all-cause mortality, a 0.55% increase in cardiovascular mortality, and a 0.74% increase in respiratory mortality.

What makes this study remarkable – despite decades of previous similar studies – is its size and the implications of a curvilinear shape in its concentration-response relation, according to Dr. Balmes.

"The current study of PM data from many regions around the world provides the strongest evidence to date that higher levels of exposure may be associated with a lower per-unit risk," Dr. Balmes wrote. "Regions that have lower exposures had a higher per-unit risk. This finding has profound policy implications, especially given that no threshold of effect was found. Even high-income countries, such as the United States, with relatively good air quality could still see public health benefits from further reduction of ambient PM concentrations."

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SOURCE: Liu C et al. N Engl J Med. 2019;381:705-15.

Transient opioid use linked to COPD exacerbation

BY JENNIFER SMITH
MDedge News

Short-term opioid use is associated with acute respiratory exacerbation in adults with chronic obstructive pulmonary disease (COPD), according to a study of Medicaid claims data.

The data showed that opioid exposure in the prior 7 days was significantly associated with acute respiratory exacerbation. The odds of exacerbation increased as the morphine-equivalent daily dose increased and as the exposure window decreased.

These results "underline the immediacy of the risk of opioid use," according to Yiran Rong of the department of pharmacy administration at the University of Mississippi in Jackson and colleagues. Ms. Rong and colleagues reported their findings in the American Journal of Epidemiology.

The researchers analyzed Mississippi Medicaid administrative claims data from 2013 to 2017, which included 1,354 beneficiaries with 1,972 exacerbation events. The beneficiaries had a mean age of 53.11 years, 69.9% were female, and 59.7% were white. The patients had an average of 1.46 exacerbation events, and 62.27% of these events occurred in patients who had an opioid prescription filled in the previous 7 days.

The researchers compared the frequency and dose of opioid exposure in the 7 days before an exacerbation to the opioid exposure in 10 control periods, each 7 days long.

Opioid exposure in the prior 7 days was associated with an 80.8% increase in the odds of exacerbation. The odds ratio, adjusted for exposure to bronchodilators, corticosteroids, benzodiazepines, and beta-blockers, was 1.81 (95% confidence interval, 1.60-2.05).

Opioid exposure was associated with exacerbation in patients with a single exacerbation event (OR, 1.91; 95% CI, 1.61, 2.27), multiple events (OR, 1.71; 95% CI, 1.45-2.01), events recorded in the emergency department (OR, 2.01; 95% CI, 1.71-2.35), and events recorded in the hospital (OR, 1.47; 95% CI, 1.21-1.79).

The odds of exacerbation increased as the morphine-equivalent daily dose increased. Each 25-mg increase in morphine-equivalent daily dose was associated with an 11.2% increase in the odds of exacerbation (OR, 1.11; 95% CI, 1.04-1.20).

"This dose-response relationship is consistent with previously established evidence … and is indicative of the need for caution in prescribing high doses of opioids to COPD patients," the researchers wrote.

They also found the odds of exacerbation increased as the exposure window decreased. The OR was 1.74 (95% CI, 1.54-1.97) for opioid exposure in an 8-day window before exacerbation and 2.00 (95% CI, 1.73-2.30) for opioid exposure in a 5-day window before exacerbation.

This suggests that "opioid-induced respiratory depression has a very short-term onset," according to the researchers.

The team noted that this study has limitations, including its retrospective, observational nature, but the results suggest transient opioid use is associated with acute respiratory exacerbation of COPD.

There was no funding for this study, and none of the researchers declared conflicts of interest.

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SOURCE: Rong Y et al. Am J Epidemiol. 2019 Jul 30. doi: 10.1093/aje/kwz169.

LIDERINA/THINKSTOCK

VIEW ON THE NEWS

Daniel Ouellette, MD, FCCP, comments: Nearly 30% of patients admitted with COPD exacerbations to the city hospital where I practice will be readmitted with the same diagnosis within a few weeks after discharge. The government and insurance companies view COPD readmissions as a failed quality metric. My colleagues and I know that our inner-city patients with COPD are confronted by medication expense, lack of transportation to outpatient venues, multiple comorbidities, and poor health-related literacy. Despite a state crackdown on opioid prescriptions by providers, our patients with COPD frequently use and misuse prescription opioids. Knowing that COPD exacerbations are linked to opioid use is important new information for my practice. It will be interesting to learn why this is so and challenging to change physician and patient practices.

COPD eosinophil counts predict steroid responders

BY WILL PASS
MDedge News

Triple therapy with an inhaled corticosteroid is particularly helpful for patients with chronic obstructive pulmonary disease (COPD) who have high baseline eosinophil counts, a trial involving more than 10,000 patients found.

Former smokers received greater benefit from inhaled corticosteroids (ICS) than did current smokers, reported lead author Steven Pascoe, MBBS, of GlaxoSmithKline and colleagues. The investigators noted that these findings can help personalize therapy for patients with COPD, which can be challenging to treat because of its heterogeneity. The study was published in Lancet Respiratory Medicine.

The phase 3 IMPACT trial compared single-inhaler fluticasone furoate–umeclidinium–vilanterol with umeclidinium-vilanterol and fluticasone furoate–vilanterol in patients with moderate to very severe COPD at high risk of exacerbation. Of the 10,333 patients involved, approximately one-quarter (26%) had one or more severe exacerbations in the previous year and half (47%) had two or more moderate exacerbations in the same time period. All patients were symptomatic and were aged 40 years or older. A variety of baseline and demographic patient characteristics were recorded, including blood eosinophil count, smoking status, and others. Responses to therapy were measured with trough forced expiratory volume in 1 second (FEV_1), symptom scoring, and a quality of life questionnaire.

After 52 weeks, results showed that higher baseline eosinophil counts were associated with progressively greater benefits in favor of triple therapy. For patients with baseline blood eosinophil counts of at least 310 cells per mcL, triple therapy was associated with about half as many moderate and severe exacerbations as treatment with umeclidinium-vilanterol (rate ratio = 0.56; 95% confidence interval, 0.47-0.66). For patients with less than 90 cells per mcL at baseline, the rate ratio for the same two regimens was 0.88, but with a confidence interval crossing 1 (0.74-1.04). For fluticasone furoate–vilanterol

Continued on following page

Continued from previous page

vs. umeclidinium-vilanterol, high baseline eosinophil count again demonstrated its predictive power for ICS efficacy, again with an associated rate ratio of 0.56 (0.47-0.66), compared with 1.09 (0.91-1.29) for patients below the lower threshold. Symptom scoring, quality of life, and FEV_1 followed a similar trend, although the investigators noted that this was "less marked" for FEV_1. Although the trend held regardless of smoking status, benefits were more pronounced among former smokers than current smokers.

For patients with baseline blood eosinophil counts of at least 310 cells per mcL, triple therapy was associated with about half as many moderate and severe exacerbations as treatment with umeclidinium-vilanterol.

"In former smokers, ICS benefits were observed at all blood eosinophil counts when comparing triple therapy with umeclidinium-vilanterol, whereas in current smokers no ICS benefit was observed at lower eosinophil counts, less than approximately 200 eosinophils per [mcL]," the investigators wrote.

"Overall, these results show the potential use of blood eosinophil counts in conjunction with smoking status to predict the magnitude of ICS response within a dual or triple-combination therapy," the investigators concluded. "Future approaches to the pharmacological management of COPD should move beyond the simple dichotomization of each clinical or biomarker variable, toward more complex algorithms that integrate the interactions between important variables including exacerbation history, smoking status, and blood eosinophil counts."

The study was funded by GlaxoSmithKline. The investigators disclosed additional relationships with AstraZeneca, Boehringer Ingelheim, Chiesi, CSA Medical, and others.

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SOURCE: Pascoe S et al. Lancet Resp Med. 2019 Jul 4. doi: 10.1016/S2213-2600(19)30190-0.

VIEW ON THE NEWS

Eric J. Gartman, MD, FCCP, comments: As more information on phenotyping patients with COPD is made available, it becomes quite evident that the "one-size-fits-all" approach to treatment no longer applies. In the near future, our patients will benefit from personalized approaches to medication class selection, drug delivery optimization, and adjustments in treatment strategy and aggressiveness based on measured biomarkers. This research describes a broad phenotype that will be more likely to benefit from inhaled corticosteroids, and marks an important turning point in our approach to patients – one where we are looking beyond spirometry, symptoms, and exacerbation history – and more toward personalization. This type of approach will only become more finely tuned as time progresses and hopefully, will result in more effective individualized treatment.

New COPD subtypes help refine risk

BY JENNIE SMITH
MDedge News

FROM THE JOURNAL *CHEST*® ▪ Chronic obstructive pulmonary disease (COPD) is often heterogeneous in its presentation and prognosis, and neither pulmonary function tests nor CT alone are always adequate to characterize a patient's disease. Combining visual and quantitative information from these clinical tests, however, can allow physicians to more precisely subtype COPD and assess patients' risk, a study has found.

In a paper published in CHEST, Jinkyeong Park, MD, PhD, of Dongguk University Ilsan Hospital in Goyang, South Korea, and colleagues looked at data from 9,080 subjects enrolled in the COPDGene study, an observational cohort of longtime smokers with and without

COPD. By assessing visually defined patterns of emphysema with quantitative imaging features and spirometry data, the researchers identified 10 distinct subtypes of COPD (including no disease) and noted significant differences in mortality and progression among them.

Dr. Park and colleagues found that patients in the subgroups with quantitative but no visual emphysema and those with visual but not quantitative emphysema represented unique groups with mild COPD that were both at risk for progression – but with likely different underlying mechanisms. Current smokers, women, and whites were more common among subjects showing visually defined emphysema without quantitative evidence. "Many of the subjects in the visual-only emphysema subtype have areas of low lung density due to emphysema masked by smoking-induced lung inflammation," the researchers wrote.

Overall 5-year mortality differed significantly among the groups (*P* less than .01) and was highest in the three groups with moderate to severe centrilobular emphysema. Patients with paraseptal and moderate to severe centrilobular emphysema showed substantial progression of emphysema over 5 years, compared with individuals with no CT abnormality (*P* less than .05).

"These results suggest that the combination of visual and quantitative CT features, which may reflect different underlying pathobiological processes in COPD, may provide a superior approach to classify individuals with COPD, compared to the use of visual or quantitative CT features alone," the researchers wrote.

By assessing visually defined patterns of emphysema with quantitative imaging features and spirometry data, the researchers identified 10 distinct subtypes of COPD (including no disease).

The study received funding from the National Heart, Lung, and Blood Institute. Three of the study's coauthors reported conflicts of interest in the form of patent applications or financial support from pharmaceutical firms. The COPDGene Project receives pharmaceutical industry and U.S. government support.

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SOURCE: Park J et al. CHEST. 2019 Jul 5. doi:10:1016/j.chest.2019.06.15.

VIEW ON THE NEWS

Eric J. Gartman, MD, FCCP, comments: It is clear that no one instrument adequately phenotypes a patient with COPD – whether one is addressing symptom burden, exacerbation risk, or disease progression. Development of tools such as those described in this study are needed so that we may better characterize a patient's disease burden and more accurately provide useful prognostication to patients. Further, if future work leads to the development of reliable risk models, they may serve as another modality that can not only be used for patient information but also for motivation for lifestyle changes (i.e. smoking cessation).

Half of sudden cardiac deaths tied to prior silent MI

BY NICOLA GARRETT
MDedge News

Almost half of individuals who died of sudden cardiac death (SCD) had a myocardial scar at autopsy, indicating a prior silent myocardial infarction (SMI), in a case-controlled study.

The research team led by Juha H. Vähätalo, MD, from the University of Oulu (Finland), compared autopsy findings, clinical characteristics, and ECG markers associated with SMI in 5,869 people in Northern Finland who had SCDs during 1998-2017.

CATHY YEULET/THINKSTOCK

Overall, 75% of the deaths were caused by coronary artery disease (CAD), and of them, 71% had no previous diagnosis of CAD. Of these latter individuals, 42% had a myocardial scar at autopsy (detected by macroscopic and microscopic evaluation of myocardium), a finding that the authors said indicated a previous, unrecognized MI.

The analysis showed that individuals with SMI were slightly older, at 69.9 years, than were those with no SMI, at 65.5 years, and were more likely to be male (83.4% vs. 75.5%).

The group with prior SMI also died during physical activity at a greater rate than did those without (18.2% vs. 12.4%), the study authors reported in their paper published in JAMA Cardiology.

The research team obtained 438 ECGs prior to SCD; 187 in individuals with SMI and 251 in the group previously diagnosed with CAD.

Of the premortem ECGs in the individuals who had had an SCD after an SMI, 67% were abnormal, the researchers reported.

The SMI group had more frequently inverted T waves (16.6% vs. 8.4%) and pathologic Q waves (12.8% vs. 6.8%), compared with the non-SMI group. Both differences were statistically significant.

Fragmented QRS was the most common marker of a scar in the SMI group, however the authors noted that the fQRS complex was "probably a sensitive marker of myocardial scarring, but its specificity is not very high".

Overall, having at least one of the following ECG abnormalities – fQRS, Q wave, T-wave inversion, or QRS of at least 110 milliseconds – was more common in the SMI group (66.8%), compared with the non-SMI group (55.4%).

"Among patients in whom SCD without a prior MI is the first sign of cardiac disease, a previous ECG result is likely to be normal. ... ECGs were available only in 187 individuals with SMI, so the data are not sufficient to draw definite conclusions. Rather, they support motivation for further studies on this question," the study authors noted.

"In the future, other, more efficient methods might be useful for diagnosing SMI, in addition to standard ECGs," such as cardiac MRI, but the cost-effectiveness "is likely to be unreasonable. Therefore, screening high-risk populations with ECG to identify individuals for further examinations would probably be reasonable," they wrote.

The research team noted some limitations of the study such as the autopsy data not revealing the size of the scar detected in the myocardium and not all individuals had an ECG recorded prior to death.

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SOURCE: Vähätalo JH et al. JAMA Cardiol. 2019 Jul 10. doi: 10.1001/jamacardio.2019.2210.

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments: It has been a long-held belief that the majority of SCD are caused by ischemic heart disease. The present study puts further proof to this belief by looking at the autopsy findings in SCD victims.

No drop in PE risk with vena cava filters after severe injury

BY BIANCA NOGRADY
MDedge News

MELBOURNE – Use of a prophylactic vena cava filter to trap blood clots in severely injured patients does not appear to reduce the risk of pulmonary embolism or death, according to data presented at the International Society on Thrombosis and Haemostasis congress.

The researchers reported the outcomes of a multicenter, controlled trial in which 240 severely injured patients with a contraindication to anticoagulants were randomized to receive a vena cava filter within 72 hours of admission, or no filter. The findings were published simultaneously in the New England Journal of Medicine.

The study showed no significant differences between the filter and no-filter groups in the primary outcome of a composite of symptomatic pulmonary embolism or death from any cause at 90 days after enrollment (13.9% vs. 14.4% respectively, $P = .98$).

In a prespecified subgroup analysis, researchers examined patients who survived 7 days after injury and did not receive prophylactic anticoagulation in those 7 days. Among this group of patients, none of those who received the vena cava filter experienced a symptomatic pulmonary embolism between day 8 and day 90, but five patients (14.7%) in the no-filter group did.

Filters were left in place for a median duration of 27 days (11-90 days). Among the 122 patients who received a filter – which included 2 patients in the control group – researchers found trapped thrombi in the filter in 6 patients.

Transfusion requirements, and the incidence of major and nonmajor bleeding and leg deep vein thrombosis, were similar between the filter and no-filter groups. Seven patients in the filter group (5.7%) required more than one attempt to remove the filter, and in one patient the filter had to be removed surgically.

Kwok M. Ho, PhD, of the department of intensive care medicine at Royal Perth (Australia) Hospital, and coauthors wrote that, while vena cava filters are widely used in trauma centers to prevent pulmonary embolism in patients at high risk of bleeding, there are conflicting recommendations regarding their use, and most studies so far have been observational.

"Given the cost and risks associated with a vena cava filter, our data suggest that there is no urgency to insert the filter in patients who can be treated with prophylactic anticoagulation within 7 days after injury," they wrote. "Unnecessary insertion of a vena cava filter has the potential to cause harm." They did note that patients with multiple, large intracranial hematomas were particularly at risk from bleeding with anticoagulant therapy, and therefore may benefit from the use of a vena cava filter.

The Medical Research Foundation of Royal Perth Hospital and the Western Australian Department of Health funded the study. Dr. Ho reported funding from the Western Australian Department of Health and the Raine Medical Research Foundation to conduct the study, as well as serving as an adviser to Medtronic and Cardinal Health.

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SOURCE: Ho KM et al. N Engl J Med. 2019 Jul 7. doi: 10.156/NEJMoa1806515.

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments: This study was carried out in severely injured patients with an Injury Severity Score >15 (median score 27). The results are informative and support the American College of Chest Physicians recommendation on patients with major trauma that states, "8.4.4. For major trauma patients, we suggest that an IVC filter should not be used for primary VTE prevention (Grade 2C); (CHEST. 2012 Feb; 141[2 Suppl]: 7S–47S).

Enteral feeding is safe during bronchiolitis HFNC

BY M. ALEXANDER OTTO
MDedge News

SEATTLE – There were no cases of aspiration with enteric feeds of 60 children aged up to 2 years on high flow nasal cannula (HFNC) for bronchiolitis at the University of Oklahoma Children's Hospital, Oklahoma City, according to research presented at Pediatric Hospital Medicine.

HFNC has become common for bronchiolitis management; it often saves infants from mechanical ventilation. However, many providers opt for total parenteral nutrition during therapy instead of enteral feeding because of concerns about aspiration pneumonia.

Pediatricians at the children's hospital began to wonder if the concern was really necessary. There have been reports of safe feeding during HFNC, and "clinical care literature has shown that feeding the gut throughout illness improves outcomes," said lead investigator Sarah Walter, MD, a third-year pediatrics resident at the hospital.

The researchers consulted the HFNC literature, asked their fellow providers what they would be comfortable with, and instituted a pediatric HFNC enteral feeding protocol at the children's hospital for use on inpatient floors, pediatric ICUs, and elsewhere.

Feedings – formula or breast milk – are triggered by stable respiratory Tal scores over 8 hours, meaning

M. Alexander Otto/MDedge News

Dr. Sarah Walter

that respiratory rates, breath sounds, and accessory muscle use were stable or improving. Children on a flow of 6 L/min or less, with a respiratory rate below 60 breaths per minute, are started on oral feeds, and those on higher flows on nasogastric (NG) tube feeds.

Feeds are started at 1 mL/kg per hour and advanced by the same amount every 3 hours until volume goals are reached; intravenous fluids are tapered accordingly. It's a standing order, so nurses are able to initiate and advance feeding as indicated, any time of day.

Feeding was temporarily suspended in only 17 children: 6 for emesis, 6 for worsening respiratory scores, and the rest for dislodged NG tubes, procedures, or other issues. Enteric feeds were restarted with two stable scores below 7 points, at half the rate at which they were stopped.

NG tubes were used in over half of the 478 nursing shifts during which the 60 children – the majority aged 4-24 months – were fed; oral feeds in more than a third; and gastric tubes and other options in the rest. Intravenous nutrition was used during just 1.8% of the shifts.

Enteric feeds were given up to a flow rate of 3.5 L/kg. There were no aspirations, even when children vomited. "We have seen good results so far that feeding is safe in these children," Dr. Walters said.

"Our hospitalist team has been very receptive; they have been using the order set pretty continuously." Parents also feel better when they know their children were getting nourishment, even if by NG tube. "It's important for family satisfaction," she said.

The next step is to assess impact on length of stay, and education efforts to encourage broader use of the order set.

There was no external funding, and Dr. Walter had no disclosures. The meeting was sponsored by the Society of Hospital Medicine, the American Academy of Pediatrics, and the Academic Pediatric Association.

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VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments: More research in the use and safety of high-flow nasal cannula in pediatrics is very much needed for all age groups. Parent satisfaction with treatment regimens is also important to study.

Short-course azithromycin no benefit in pediatric asthma

BY M. ALEXANDER OTTO
MDedge News

SEATTLE – Adding a 3-day course of azithromycin to treatment regimens of children hospitalized with asthma did not shorten length of stay or bring other benefits in a randomized, blinded trial of more than 150 children at the Children's Hospital at Montefiore, New York.

In recent years, some pediatricians at Montefiore had begun giving short-course azithromycin to hospitalized children who were not recovering as quickly as they had hoped, spurred by outpatient reports of reduced exacerbations and other benefits with long-term azithromycin (e.g., Lancet. 2017 Aug 12;390(10095):659-68).

"We had no evidence for doing that at all" in the hospital, and it might be going on elsewhere, said senior investigator Alyssa Silver, MD, assistant professor of pediatrics at Montefiore and Albert Einstein College of Medicine, New York. She and her team took a closer look.

The negative results mean that "we can stop doing this, giving kids unnecessary things. Word is starting to get out" at Montefiore. "People are not using it as much," she said at Pediatric Hospital Medicine, sponsored by the Society of Hospital Medicine, the American Academy of Pediatrics, and the Academic Pediatric Association.

M. Alexander Otto/MDedge News

Dr. Alyssa Silver

The team had expected azithromycin to shorten length of stay (LOS) by about half a day, because of its anti-inflammatory effects, but that's not what was found when they randomized 80 children aged 4-12 years with persistent asthma to oral azithromycin 10 mg/kg per day for 3 days within 12 hours of admission, and 79 to placebo.

LOS was 1.86 days in the placebo arm, and 1.69 days in the azithromycin group ($P = .23$). One placebo child was transferred to the pediatric ICU, versus none in the azithromycin arm ($P = .50$). The study was stopped short of its 214 subject enrollment goal because of futility, but even so, it was well powered to detect a difference in LOS, the primary outcome, Dr. Silver said.

At 1-week phone follow-up, 7 placebo children and 11 in the azithromycin arm had persistent asthma symptoms ($P = .42$), and 1 placebo child and 2 azithromycin children had been readmitted (P greater than .99). There were no differences in days of school missed, or workdays missed among parents and guardians. At 1 month, 23 placebo and 18 azithromycin children had persistent asthma symptoms ($P = .5$); 7 placebo and 6 azithromycin children had returned to the ED ($P = .75$).

In short, "we really found no difference" with short-course azithromycin. "Clinicians should consider [these] data before prescribing azithromycin [to] children hospitalized with asthma," Dr. Silver and her team concluded.

There was no external funding, and Dr. Silver had no disclosures.

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VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments: This study is very important because azithromycin has become popular for many reasons. For example, there is published research in cystic fibrosis for azithromycin used chronically for patients colonized with Pseudomonas. Clinicians also use it for its anti-inflammatory properties in other pediatric and adult pulmonary conditions. This is a fairly large study that trialed the drug acutely as an anti-inflammatory. The negative results are very informative.

COPD adds complexity to shared decision making for LDCT lung cancer screening

BY BIANCA NOGRADY

FROM THE JOURNAL *CHEST* ▪ Shared decision making (SDM) around low-dose computed tomography (LDCT) screening for lung cancer should include risk and benefit information for patients with baseline conditions such as chronic obstructive pulmonary disease (COPD), research suggests.

Jonathan M. Iaccarino, MD, of the pulmonary center at Boston University and coauthors reported the results of a secondary analysis of LDCT-level versus patient-level outcomes from 75,138 LDCT scans in 26,453 participants in the National Lung Screening Trial (NLST) in CHEST (2019 Jul 5. doi: 10.1016/j.chest.2019.06.016).

Currently, LDCT screening is recommended annually for high-risk smokers aged 55-80 years. The NLST showed that screening with LDCT achieved a 20% relative reduction in lung cancer mortality and 6.7% relative reduction in overall mortality in this group. Screening guidelines stress the importance of shared decision making, with discussion of the risks and benefits of screening.

Dr. Iaccarino and colleagues point out that decision aids for SDM need to include important baseline characteristics, such as the presence of COPD, because these can complicate the risk and benefit analysis.

At the LDCT-level outcomes, 14.2% of the 75,138 LDCT scans performed during the 3-year NLST study period led to a subsequent diagnostic study and 1.5% resulted in an invasive procedure. In addition, 0.3% of scans resulted in a procedure-related complication, and in 89 cases (0.1%), this procedure-related complication was serious. At the patient-level outcomes, nearly one-third (30.5%) of the 26,453 participants who underwent screening over 3 years received a diagnostic study, 4.2% underwent an invasive procedure (41% of whom ultimately were found not to have lung cancer), 0.9% had a procedure-related complication, and 0.3% had a serious procedure-related complication. Furthermore, among those who experienced a serious complication, 12.5% were found not to have lung cancer.

The authors compared outcomes in patients with and without COPD and found that the 4,632 participants with self-reported COPD were significantly more likely to undergo diagnostic studies (36.2%), have an invasive procedure (6%), experience a procedure-related complication (1.5%), and experience a serious procedure-related complication (0.6%) than were participants without COPD. However, they also had a significantly higher incidence of lung cancer diagnosis than did participants without COPD (6.1% vs. 3.6%).

"Our study analyzes cumulative outcomes at the level of the individual patient over the three years of LDCT screening during the NLST, showing higher rates of diagnostic procedures, invasive procedures, complications and serious complications than apparent when data is presented at the level of the individual test," the authors wrote.

"While most decision aids note the risks of screening may be increased in those with COPD, our study helps quantify these increased risks as well as the increased likelihood of a lung cancer diagnosis, a critical advance given that providing personalized (rather than generic) information results in more accurate risk perception and more informed choices among individuals considering screening," the authors wrote. "With the significant change in the balance of benefits and risks of screening in patients with COPD, it is critical to adjust the shared decision-making discussions accordingly."

They also noted that other comorbidities, such as heart disease, vascular disease, and other lung diseases, would likely affect the balance of risk and benefit of LDCT screening and that there was a need for further exploration of screening in these patients.

Noting the study's limitations, the authors pointed that their analysis focused on outcomes that were not the primary outcomes of the National Lung Screening trial and that they relied on self-reported COPD diagnoses.

The study was supported by the American Society of Clinical Oncology, the Charles A. King Trust, and Edith Nourse Rogers Memorial Veterans Hospital. No conflicts of interest were declared.

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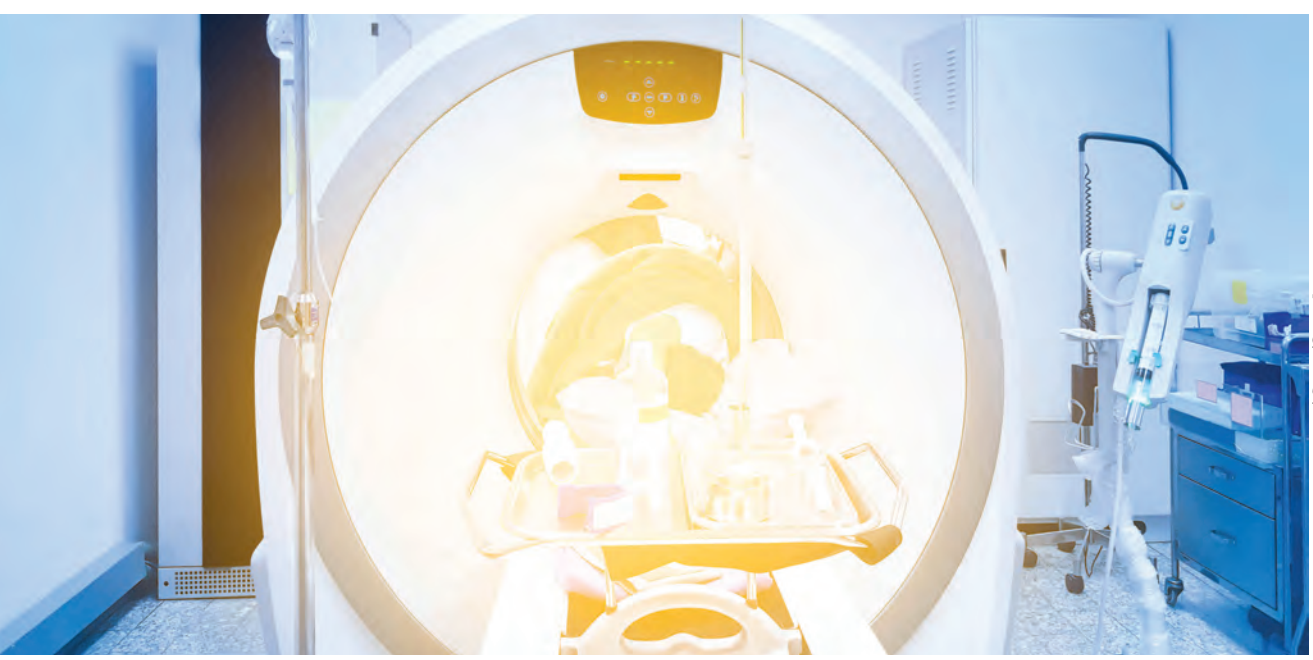
SOURCE: Iaccarino JM et al. CHEST. 2019 Jul 5. doi: 10.1016/j.chest.2019.06.016.

VIEW ON THE NEWS

M. Patricia Rivera, MD, FCCP, comments:

A significant challenge in lung cancer screening (LCS) implementation is how to incorporate the impact comorbid diseases may have on the benefit-harm ratio of screening. Furthermore, how the balance of benefits and risks may change over a prolonged period of screening is largely unknown. The study by Iaccarino et al. analyzed outcomes for each LDCT performed in the NLST over 3 years of screening and also compared outcomes between patients with and without COPD. Results showed that, throughout multiple years of screening, rates of diagnostic procedures, invasive procedures, complications, and serious complications were higher when compared with data presented at the level of one individual test. In most patients, LCS will be conducted over many years (if a patient starts at age 55 and goes to age 80, he/she will undergo screening for 25 years); thus, the cumulative risk of screening may be underestimated. The study also demonstrates how comorbidities, particularly COPD, can impact the benefits and risks of screening - over 3 years of screening in the NLST, which enrolled fairly healthy individuals, patients with COPD had higher odds of needing an invasive procedure and having complications from screening-related procedure while at the same time having higher rates of lung cancer. It is important to understand how the balance of benefits and risks of LCS may shift over cumulative screening and because of underlying comorbidities in the real-world setting of LCS, in which the population eligible for screening is older and more likely to have advanced comorbidities when compared with the NLST participants. Moreover, this knowledge will be essential in order to aid providers in personalizing and framing the shared decision-making discussions.



MR.SUPHACHAI PRASERDUMRONGCHAI/ISTOCK/GETTY IMAGES

ICS treatment for COPD may lower lung cancer risk

BY JEFF CRAVEN
MDedge News

Use of inhaled corticosteroids (ICS) may lower the risk of lung cancer in patients with chronic obstructive pulmonary disease (COPD), and continued use may also reduce lung cancer risk, recent research from the European Respiratory Journal has shown.

"The appropriate use of ICS in COPD patients is often debated and not all patients might benefit from the use of ICS. The clinical benefits and risk of use in an individual patient must be weighed by the physician," wrote Adam J.N. Raymakers, MSc, PhD, of the University of British Columbia's Collaboration for Outcomes Research and Evaluation (CORE), Vancouver, and colleagues.

"This study, however, indicates that potential benefits may accrue from ICS use in COPD patients in terms of reduced lung cancer risk, and that sustained use may be associated with reduced risk of lung cancer."

Dr. Raymakers and colleagues did an analysis of 39,676 patients with COPD (mean age, 70.7 years; 53% female) who received ICS between 1997 and 2007 and linked those patients to a registry of cancer patients in British Columbia. The linked databases included the Medical Services Plan payment information file, Discharge Abstract Database, PharmaNet data file, and the British Columbia Cancer Registry. The researchers determined a patient had COPD if he or she received three or more prescriptions related to COPD, while ICS exposure was analyzed in the context of a patient's ICS exposure, cumulative duration, cumulative dose, and weighted cumulative duration and dose.

The analysis revealed 372,075 prescriptions for ICS were dispensed and 71.2% of the patients were "distinct users" of ICS, with patients filling a median of eight prescriptions at mean 5.2 years of follow-up. Fluticasone propionate was the most common ICS prescribed at a dose of 0.64 mg per day, and patients had median 60 days of ICS supplied per person.

Overall, there were 994 cases of lung cancer (2.5%), and exposure to ICS was linked to a 30% reduction in lung cancer risk (hazard ratio, 0.70; 95% confidence interval, 0.61-0.80), while recency-weighted duration of ICS exposure was linked to a 26% reduction in lung cancer risk (HR, 0.74; 95% CI, 0.66-0.87). There was a 43% reduced risk of lung cancer per gram of ICS when the data were measured by recency-weighted cumulative dosage.

In a multivariate analysis, ICS use was associated with a 30% reduction in risk of non–small cell lung cancer (HR, 0.70; 95% CI, 0.60-0.82), which the researchers said suggests ICS provides a protective effect for patients against lung cancer. "These results highlight the importance of properly identifying which patients might be at the highest risk of lung cancer, to enhance the therapeutic benefits of ICS in these COPD patients," they wrote.

"This study ... indicates that potential benefits may accrue from [inhaled corticosteroid] use in COPD patients in terms of reduced lung cancer risk, and that sustained use may be associated with reduced risk of lung cancer."

This study received funding from the Canadian Institutes of Health Research. The authors report no conflicts of interest.

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SOURCE: Raymakers AJN et al. Eur Respir J. 2019. doi: 10.1183/13993003.01257-2018.

VIEW ON THE NEWS

M. Patricia Rivera, MD, FCCP, comments: Chronic inflammation in COPD may be a driver in lung cancer development by increasing cell proliferation and oncogene activation. The use of anti-inflammatory drugs such as inhaled corticosteroids (ICS) as preventive treatment against lung cancer in patients with COPD has been previously studied. The results, however, have been conflicting with one study showing lower risk of lung cancer in patients with COPD taking ICS (AJRCCM. 2007;175:712-89), while a retrospective analysis did not identify a protective effect from ICS in patients with chronic airway inflammation (Lung. 2018;196:179-84). A prospective trial evaluating the effect of ICS on lung dysplasia also yielded negative results (Clin Cancer Res. 2004;10:6502-11). Raymakers et al. conducted a retrospective study of patients with COPD who received ICS and then linked those patients to a regional cancer registry. Cumulative duration of exposure and dose of ICS were analyzed and after multivariate analysis, the study found a 30% lung cancer risk reduction associated with ICS use. The authors acknowledge that use of administrative data limits the scope of the variables that could inform exposure-outcomes associations, for example, the patient filled their ICS prescription, but did they use it? Despite limitations, the magnitude of the association between ICS exposure and lung cancer risk consistent across all exposure metrics (duration and cumulative dose) supports existing data that ICS may play a potential chemopreventive role against lung cancer in patients with chronic airway inflammation. What about the possible risk of pneumonia due to ICS use and risk of lung cancer? In one study of COPD patients, an increased risk of lung cancer was found in ICS users with sequential pneumonia or TB, compared with non-ICS users with same infections (BMC Cancer. 2016;16:778). However, controversy exists regarding the risk of pneumonia associated with ICS use. While a 2014 Cochrane review found an increased risk of pneumonia associated with ICS use alone or in combination with a long-acting beta-agonist, results from the SUMMIT trial found no increase in the risk of pneumonia with ICS use in patients with COPD (Respir Med. 2017;131:27-34).

Sleep aids and dementia risk: Benefits, some risks

BY JENNIE SMITH
MDedge News

LOS ANGELES – While a large number of older adults take prescription and nonprescription medications to help them sleep, the effect of these medications on dementia risk is unclear, with most researchers advocating a cautious and conservative approach to prescribing.

Research is increasingly revealing a bidirectional relationship between sleep and dementia. Poor sleep – especially from insomnia, sleep deprivation, or obstructive sleep apnea – is known to increase dementia risk. Dementias, meanwhile, are associated with serious circadian rhythm disturbances, leading to nighttime sleep loss and increasing the likelihood of institutionalization.


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At the Alzheimer's Association International Conference, researchers presented findings assessing the links between sleep medication use and dementia and also what agents or approaches might safely improve sleep in people with sleep disorders who are at risk for dementia or who have been diagnosed with dementia.

Sex- and race-based differences in risk

Yue Leng, PhD, of the University of California, San Francisco, reported a link between frequent sleep medication use and later dementia – but only in white adults. Dr. Leng presented findings from the National Institutes of Health–funded Health, Aging, and Body Composition Study, which recruited 3,068 subjects aged 70-79 and followed them for 15 years. At baseline, 2.7% of African Americans and 7.7% of whites in the study reported taking sleep medications "often" or "almost always."

Dr. Leng and colleagues found that white subjects who reported taking sleep aids five or more times a month at baseline had a nearly 80% higher risk of developing dementia during the course of the study (hazard ratio, 1.79; 95% confidence interval, 1.21-2.66), compared with people who reported never taking sleep aids or taking them less frequently.

The researchers saw no between-sex differences for this finding, and adjusted for a variety of genetic and lifestyle confounders. Importantly, no significant increase in dementia risk was seen for black subjects, who made up more than one-third of the cohort.

Dr. Leng told the conference that the researchers could not explain why black participants did not see similarly increased dementia risk. Also, she noted, researchers did not have information on the specific sleep medications people used: benzodiazepines, antihistamines, antidepressants, or other types of drugs. Nonetheless, she told the conference, the findings ratified the cautious approach many dementia experts are already stressing.

"Do we really need to prescribe so many sleep meds to older adults who are already at risk for cognitive impairment?" Dr. Leng said, adding: "I am a big advocate of behavioral sleep interventions." People with clinical sleep problems "should be referred to sleep centers" for a fuller assessment before medication is prescribed, she said.

Findings from another cohort study, meanwhile, suggest that there could be sex-related differences in how sleep aids affect dementia risk. Investigators at Utah State University in Logan used data from some 3,656 older adults in the Cache County Study on Memory and Aging, an NIH-backed cohort study of white adults in Utah without dementia at baseline who were followed for 12 years.

The investigators, led by doctoral student Elizabeth Vernon, found that men reporting use of sleep medication saw more than threefold higher risk of developing Alzheimer's disease than did men who did not use sleep aids (HR, 3.604; P = .0001).

Women who did not report having sleep disturbance but used sleep-inducing medications were at nearly fourfold greater risk for developing Alzheimer's disease (HR, 3.916; P = .0001).

Ms. Vernon told the conference that, despite the finding of risk reduction for this particular group of women, caution in prescribing sleep aids was warranted.

Common sleep drugs and cognitive aging

Chris Fox, MD, a researcher at the University of East Anglia in Norwich, England, and colleagues demonstrated in 2018 that long-term exposure to anticholinergic drugs, a class that includes some antidepressants and antihistamines used to promote sleep, was associated with a higher risk of dementia, while use of benzodiazepines, a class of sedatives used commonly in older people as sleep aids, was not. (Whether benzodiazepine exposure relates to dementia remains controversial.)

At AAIC 2019, Dr. Fox presented findings from a study of 337 brains in a U.K. brain bank, of which 17% and 21% came from users of benzodiazepines and anticholinergic drugs, whose usage history was well documented. Dr. Fox and colleagues found that, while neither anticholinergic nor benzodiazepine exposure was associated with brain pathology specific to that seen in Alzheimer's disease, both classes of drugs were associated with "slight signals in neuronal loss" in one brain region, the nucleus basalis of Meynert. Dr. Fox described the drugs as causing "an increase in cognitive aging" which could bear on Alzheimer's risk without being directly causative.

Newer sleep drugs may help Alzheimer's patients

Scientists working for drug manufacturers presented findings on agents to counter the circadian rhythm disturbances seen in people with Alzheimer's disease. Margaret Moline, PhD, of Eisai in Woodcliff Lake, N.J., showed some results from a phase 2, dose-ranging, placebo-controlled study of the experimental agent lemborexant in 62 subjects aged 60-90 with mild to moderate Alzheimer's disease and sleep disturbances. (Lemborexant, an orexin receptor agonist that acts to regulate wakefulness, is being investigated in a broad range of sleep disorders.) Patients were randomized to one of four doses of lemborexant or placebo and wore a device for sleep monitoring. Nighttime activity indicating arousal was significantly lower for people in two dosage arms, 5 mg and 10 mg, compared with placebo, and treatment groups saw trends toward less sleep fragmentation and higher total sleep time, Dr. Moline told the conference.

Suvorexant (Belsomra), the only orexin receptor antagonist currently licensed as a sleep aid, is also being tested in people with Alzheimer's disease. At AAIC 2019, Joseph Herring, MD, PhD, of Merck in Kenilworth, N.J., presented results from a placebo-controlled trial of 277 patients with Alzheimer's disease and insomnia, and reported that treatment with 10 or 20 mg of suvorexant over 4 weeks was associated with about an extra half hour of total nightly sleep, with a 73-minute mean increase from baseline, compared with 45 minutes for patients receiving placebo (95% CI, 11-45; P less than .005).

Trazodone linked to slower cognitive decline

An inexpensive antidepressant used in low doses as a sleep aid, including in people with Alzheimer's disease, was associated with a delay in cognitive decline in older adults, according to results from a retrospective study. Elissaios Karageorgiou, MD, PhD, of the University of California, San Francisco, and the

Continued on page 25

Sleep disorder treatment tied to lower suicide attempt risk in veterans

BY THERESE BORDEN
MDedge News

Insomnia, sleep-related disordered breathing, and nightmares were associated with suicide attempts in a large case-control matched study of patients in the Veterans Health Administration database. In addition, treatment for sleep disorders was correlated to a reduced risk for suicide attempts.


Dr. Bishop

Todd M. Bishop, PhD, of the Center of Excellence for Suicide Prevention, Canandaigua (N.Y.) VA Medical Center, and the department of psychiatry, University of Rochester (N.Y.) Medical Center, and colleagues wrote that suicide is the 10th most frequent cause of death in the United States, and "nowhere is the suicide rate more alarming than among military veterans, who after adjusting for age and gender, have an approximately 1.5 times greater risk for suicide as compared to the civilian population."

Previous research has explored the link between sleep disturbances and suicide attempts. But less has been done to look at specific sleep problems, and little research has examined the role of sleep medicine interventions and suicide attempt risk.

The investigators conducted a study to establish the association between suicide attempts and specific sleep disorders, and to examine the correlation between sleep medicine treatment and suicide attempts. Their sample consisted of 60,102 veterans who had received care within the VHA between Oct. 1, 2012, and Sept. 20, 2014. Half of the sample had a documented suicide attempt in the medical record (n = 30,051) and half did not (n = 30,051). The overall sample was predominately male (87.1%) with a mean age of 48.6 years. More than half the sample identified as white (67.4%).

Suicide attempts, sleep disturbance, and medical and mental health comorbidities were identified via ICD codes and prescription records. The predominant sleep disorders studied were insomnia, sleep-related breathing disorder (SRBD), and nightmares. The first suicide attempt in the study period was determined to be the index date for the case-control matching.

Overall, sleep disturbances were much more prevalent among cases than controls (insomnia, 46.2% vs. 12.6%), sleep-related breathing disorder (8.6% vs. 4.8%), and nightmares (7.1% vs. 1.6%). A logistic regression analysis was undertaken to examine the relationship between specific sleep disorders and suicide attempts. Insomnia, nightmares, and SRBD were each associated with increased odds of a suicide attempt with the following odds ratios: insomnia (odds ratio, 5.62; 95% confidence interval, 5.39-5.86), nightmares (OR, 2.49; 95% CI, 2.23-2.77), and sleep-related breathing disorder (OR, 1.37; 95% CI, 1.27-1.48). A second model included known drivers of suicide attempts (PTSD, depression, anxiety disorders, schizophrenia, bipolar disorder, substance use disorder, medical comorbidity, and obesity). But after controlling for these factors, neither nightmares (OR, 0.96; 95% CI, 0.85-1.09) nor sleep-related breathing disorders (OR, 0.87, 95% CI, 0.79-0.94) remained positively associated with suicide attempt, but the association of insomnia with suicide attempt was maintained (OR, 1.51; 95% CI, 1.43-1.59).

The question of the impact of sleep medicine interventions on suicide attempts was studied with a third regression model adding the number of sleep medicine clinic visits in the 180 days prior to the suicide attempt index date as an independent variable. The variables in this model were limited to insomnia, SRBD, and nightmares. The investigators found that "for each sleep medicine clinic visit within the 6 months prior to index date the likelihood of suicide attempt is 11% less (OR, 0.89; 95% CI, 0.82-0.97)."

The limitations of the study include the lack of information on sleep treatment modalities or medications provided during the clinic visits, and the overlapping of sleep disturbance with other mental health conditions, such as alcohol dependence and PTSD. In addition, "some insomnia medications are labeled for risk of suicidal ideation and behavior, so there is some chance that the medications rather than insomnia itself were associated with the increased suicidal behavior," the investigators wrote.

In addition to an analysis of specific types of sleep disorders associated with suicide attempts, the study showed that treatment of sleep disorders may have an important role in suicide prevention. The investigators concluded: "Identifying populations at risk for suicide prior to a first attempt is an important, but difficult task of suicide prevention. Prevention efforts can be aimed at modifiable risk factors that arise early on a patient's trajectory toward a suicide attempt."

The study was supported by the VISN 2 Center of Excellence for Suicide Prevention, Canandaigua VAMC. The authors had no disclosures.

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SOURCE: Bishop TM et al. Sleep Med. 2019 Jul 25. doi: 10.1016/j.sleep.2019.07.016.

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Neurological Institute of Athens presented results derived from two cohorts: patients enrolled at the UCSF Memory and Aging Center and women enrolled in the Study for Osteoporotic Fractures (SOF) in Women. The investigators were able to identify trazodone users in the studies (with two or more contiguous study visits reporting trazodone use) and match them with control patients from the same cohorts who did not use trazodone.

Trazodone was studied because previous research suggests it increases total sleep time in patients with Alzheimer's disease without affecting next-day cognitive performance.

Trazodone-using patients in the UCSF cohort (n = 25) saw significantly less decline in Mini-Mental State Exam (MMSE) scores over 4 years, compared with nonusers (0.27 vs. 0.70 points per year; *P* = .023), an effect that remained statistically significant even after adjusting for sedative and stimulant use and the expected progression of Alzheimer's disease pathology. Importantly, the slower decline was seen only among subjects with sleep complaints at baseline and especially those whose sleep improved over time, suggesting that the cognitive benefit was mediated by improved sleep.

In the SOF cohort of 46 trazodone users matched with 148 nonusers, no significant protective or negative effect related to long-term trazodone use was found using the MMSE or the Trails Making Test. In this analysis, however, baseline and longitudinal sleep quality was not captured in the group-matching process, and neither was the use of other medications. The patient group was slightly older, and all patients were women.

Dr. Karageorgiou said in an interview that the link between improved sleep, trazodone, and cognition needs to be validated in prospective intervention studies. Trazodone, he said, appears to work best in people with a specific type of insomnia characterized by cortical and behavioral hyperarousal, and its cognitive effect appears limited to people whose sleep improves with treatment. "You're not going to see long-term cognitive benefits if it's not improving your sleep," Dr. Karageorgiou said. "So, whether trazodone improves sleep or not in a patient after a few months can be an early indicator for the clinician to continue using it or suspend it, because it is unlikely to help their cognition otherwise."

He stressed that physicians need to be broadly focused on improving sleep to help patients with, or at risk for, dementia by consolidating their sleep rhythms.

"Trazodone is not the magic bullet, and I don't think we will ever have a magic bullet," Dr. Karageorgiou said. "Because when our brain degenerates, it's not just one chemical, or one system, it's many. And our body changes as well. The important thing is to help the patient consolidate their rhythms, whether through light therapy, daily exercise, cognitive behavioral therapy for insomnia, or other evidence-based interventions and their combination. The same applies for a person with dementia as for the rest of us."

None of the investigators outside of the industry-sponsored studies had relevant disclosures.

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ENVIRONMENTAL SCAN

Drivers of change in technology

BY THERESE BORDEN

Emerging technology has long been a driver of change in health care, and the pace of technological change has accelerated dramatically in the past decade. Physicians are being challenged to incorporate blockchain technology, virtual health care, artificial intelligence, gamification of learning, and the rapidly developing Internet of Things into their work and into their interactions with patients.

CHEST INSPIRATION: Pacing the Future

Blockchain in health care

Blockchain is a log of activity that is time-stamped, tamper proof, and shared across a network of computers. Each transaction that goes into the log of activity is enclosed in a block and linked together in chronological order to form a chain, now called blockchain.

The potential applications of this emerging technology in health-care delivery are almost limitless.[1] Shared, secure, and linked data that can be accessed by all can give rise to the automation of complex problems, community-generated solutions to problems that empower patients, and an increase in trust, transparency, and incentive alignment. Currently, insurance claims, prescriptions, and payments mostly reside in sequestered computer systems, but a blockchain of the transactions among them would open up a wealth of learning and efficiency possibilities.[2] Hospitals, medical centers, insurance companies, clinical trials, and large practices can collaborate to create a blockchain of transactions in which all members can view access, share, and analyze the data.

Burton Lesnick, MD, FCCP, has given the topic of technology change and the practice of medicine some thought. He is a member of the CHEST Board of Regents and the former founding medical director of The Children's Care Network, a pediatric accountable care organization of 1,800 providers in metro Atlanta area. Dr. Lesnick notes that blockchain is still in its early phases, partly because it is expensive in terms of computing power and electricity to adequately maintain a distributed ledger.


Dr. Lesnick

"I would see [blockchain technology] being used in the next decade for high-value public registries, especially where the authenticity of data is critical. For instance, in Europe, we are already seeing a lot of effort to prevent counterfeit drugs from entering the pharmacy chain. We may soon see blockchain being used to track expensive drugs in our health-care system, thus ensuring chain of possession and preventing fraud," he said.

Virtual care

Some traditional face-to-face encounters between doctor and patient will be replaced by virtual care of different types. Telemedicine is growing, thanks in part to advocacy from Medicare and Medicaid, although the lack of federal guidance on coverage and reimbursement could be a barrier.[3] mHealth, the delivery of care via mobile devices, is being utilized for preventive services, appointment confirmation, and follow-up information, but the future of this technology will probably expand into transmission of data from patients and health devices, as well as health alerts.

According to a report by the World Health Organization, an increasing proportion of the population is accessing health information and services through mobile phones.[4] According to the Physicians Practice 2018 Mobile Health Survey, a majority of practices that participated in the study stated they use mobile health in their practice on a weekly basis.[5] Those still not using mHealth cite concerns over HIPAA compliance. Dr. Lesnick offers some cautionary perspectives.

"Many of us can already download data from medical devices such as CPAP machines and home ventilators. A prominent pharmaceutical company has recently gained FDA approval for an inhaler that date and time stamps when and how the inhaler has been used. Wearable health devices, such as fitness monitors and watches that can alert users about life-threatening arrhythmias are wonderful. But the potential for physicians being overwhelmed by the incoming data flow is concerning. This is especially true when physicians are already reporting high levels of burnout associated with frustration using electronic medical record systems. We can only hope that algorithms will be developed to sift the precious stones from the digital effluent."

Despite the security concerns, health-care providers, along with the Centers for Medicare & Medicaid Services and the insurance industry, are planning to address the projected shortages in the health-care workforce with virtual care.[3]

Dr. Lesnick added, "Doctors need to be engaged at the level of their health-care systems and national organizations. Providers are needed to provide context and balance to ensure that new technology utilizes appropriate scope of practice, optimizes care, and reduces costs, while reducing burdens on caregivers."

Artificial intelligence and the Internet of Things

Artificial intelligence (AI) in health care is the use of complex algorithms and software to approximate human analysis of complicated medical data. The applications in medicine are potentially limitless given the rapid accumulation of data related to health care.

According to Forbes, AI for health-care IT application will cross $1.7 billion by 2019.[2] By operationalizing AI platforms across select health-care workflows, organizations could see significant productivity gains during the next few years. Forbes also predicts more AI solutions will be used in imaging diagnostics, drug discovery, and risk-analytics applications.[2]

At the Icahn School of Medicine at Mount Sinai, New York, researchers use an in-house AI system known as Deep Patient, to predict risk factors for 78 different diseases. Doctors use the system to aid in diagnoses.[9] AI is being used to diagnose patient wounds via smartphones, remotely monitor the elderly, and help health

systems to digitally verify a patient's insurance information.

Dr. Lesnick observed that chess computers started beating grand masters more than 20 years ago. However, the best chess players, in combination with a computer, can still reliably beat a computer alone. We need organizations like CHEST to help us become more adept at using technology. AI is a powerful tool but just another instrument to be employed in care of patients.

Big data and AI will combine to create new ways of practicing medicine in the coming years, but what this trend will mean to individual clinicians remains to seen.

An area of rapid development is the Internet of Things, the extension of internet connectivity into everyday objects and devices designed to monitor and send information. Health-care devices now incorporate AI, real-time analytics, machine learning, physiologic sensors, and embedded systems.[10] Physicians will increasingly have access to real-time data on individual patients. For physicians, managing, storing, and analyzing data from the personalized health-care devices of their patients will be a major challenge as the Internet of Things continues to expand into health care.

For physicians, managing, storing, and analyzing data from the personalized health-care devices of their patients will be a major challenge as the Internet of Things continues to expand into health care.

Dr. Lesnick noted, "In my collaboration with Georgia Tech [in Atlanta], one area I'm really excited about is process mining. Instead of sorting individual data points for statistical correlation, process mining looks at groups of actions and decisions. We've applied this to our local emergency room. I'm hoping we can find the most efficient processes and hardwire them in order sets. If we can eventually apply process mining to the health-care system as a whole, we might start to see gains in efficiencies."

Gamification

Gamification is the term used to describe any tool or platform that applies game mechanics to nongame initiatives in order to encourage and increase engagement. Elements of gamification often include the use of badges, reward points, prizes, social interaction, and leaderboards. Gamification is frequently used by sales teams, marketers, employee training and performance management, onboarding, learning management, and health and wellness.[11]

The rise in smartphone ownership and wearable technology will likely increase the adoption of gamification technologies to manage health-related concerns and issues. Patient education via gamification is a potentially powerful tool to enhance engagement around disease management. Maintenance of certification and CME are also growth areas for gamification.

Cybersecurity and data breaches

The rapid development of mobile devices and the Internet of Things, in addition to the transmission of health data on a massive scale, will mean more health data will be stolen for a variety of illegal purposes. Hacking and unauthorized access are now common occurrences. Privacy breaches, potential HIPAA violations, and financial damage to patients and institutions are all areas of concern that accompany technological changes.[12]

Dr. Lesnick stressed that all health-care professionals must be accountable for safeguarding patient information and using the latest security software. "Physicians can be advocates for their patients by cautioning them about the risks of placing their private medical information into public spaces, such as social media. Patients should also know that they may be waiving their privacy rights when they utilize commercial entities that collect and store DNA analyses for purposes of ancestry tracking or medical screening," he concluded.

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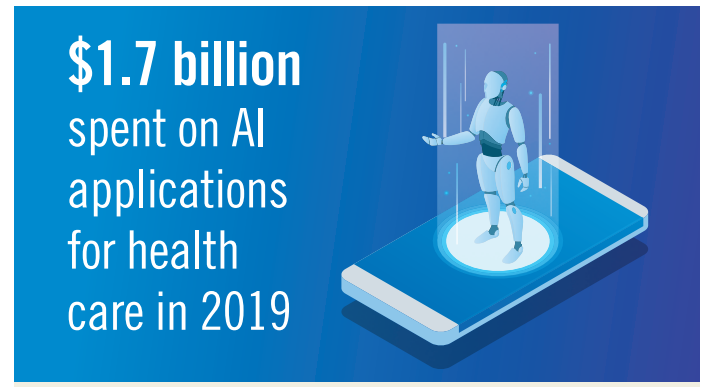

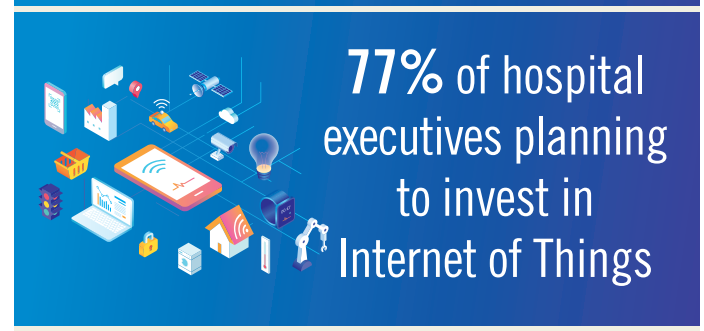

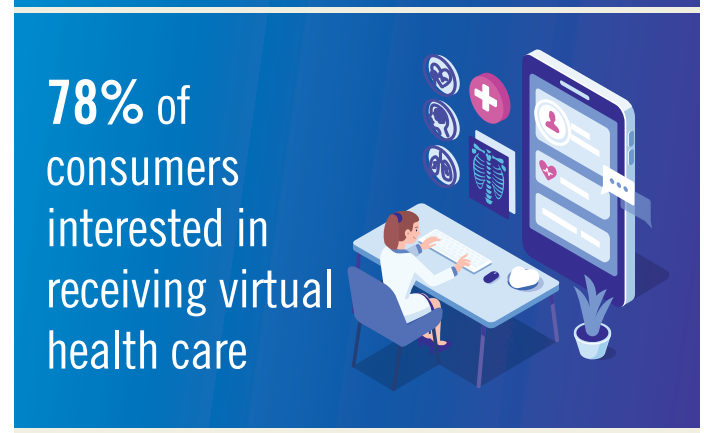

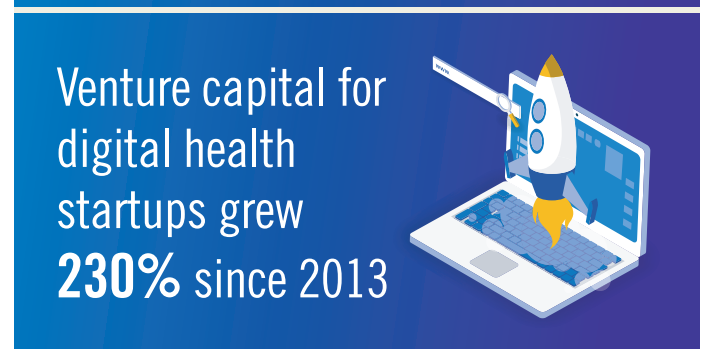

CHEST Inspiration is a collection of programmatic initiatives developed by the American College of Chest Physicians leadership and aimed at stimulating and encouraging innovation within the association. One of the components of CHEST Inspiration is the Environmental Scan, a series of articles focusing on the internal and external environmental factors that bear on success currently and in the future. See "Envisioning the Future: The CHEST Environmental Scan," *CHEST Physician*, June 2019, p. 44, for an introduction to the series.

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Getting to know our incoming CHEST President

Stephanie M. Levine, MD, FCCP, is an expert in lung transplantation, and pulmonary and critical care issues in pregnancy and women's lung health. She is a Professor of Medicine in the Division of Pulmonary Diseases and Critical Care Medicine at the University of Texas Health Science Center in San Antonio, Texas; the Program Director of the Pulmonary and Critical Care Fellowship at the University of Texas Health Science Center; and the Co-Director of the Medical Intensive Care Unit at the University Hospital. She is also a staff physician at the Audie Murphy Veteran Administration Hospital.

Our greatest strengths are the education we deliver; the people at all levels who deliver, learn from, and support the delivery of this core component of our vision and mission.

Dr. Levine has been Editor for both CHEST SEEK Critical Care Medicine and Pulmonary Medicine editions. In 2009, she received the CHEST Presidential Citation Award; in 2010, the CHEST Distinguished Service Award; and in 2017, the Master Clinician Educator Award. She has also been recognized as a Distinguished CHEST Educator in 2017, 2018, and 2019.

Dr. Levine has been active in CHEST international activities with CHEST World Congress meetings, the 2017 Basel Joint CHEST/SPG Congress in collaboration with the Swiss Lung Association, and with the pulmonary/critical care subspecialty training programs developed in China. She was President and Chair of the CHEST Foundation from 2010-2014 and is currently on the CHEST Board of Regents.

We asked Dr. Levine for some thoughts on her upcoming CHEST presidency.

What would you like to accomplish as President of CHEST?

Every 5 years, the Board of Regents sets forth a new 5-year strategic plan, which is re-evaluated annually. We try to make sure all our decisions and actions align with this strategic plan. As President, I will promote the vision and mission of CHEST while guiding our organization to succeed in our 2018-2022 strategic plan. What will this include? This will include developing new innovative, evidenced-based, education and educational products in the areas of pulmonary, critical care, and sleep medicine; producing evidence-based guidelines; and expanding our educational expertise both nationally and globally. I am committed to actively engage and retain our fellows-in-training (being a longstanding program director), and to mentor our future leaders. I will reach out to engage and educate advanced practice providers, who are an integral part of our patient care teams. We will grow the CHEST Foundation in the areas of patient education and access, clinical research funding, and community service. On the global front, we will continue with our new global strategy of holding congresses based on the annual meeting content and smaller board review format regional conferences in different parts of the world seeking education in pulmonary, critical care, and sleep medicine. Our next meeting is in Bologna, Italy, in June of 2020. I will build on our collaborative inter-societal relationships with our related societies. Some of the specific areas I plan to focus on are defining the true value of CHEST membership, engaging all members of the health-care team, and revisiting the structure and function of our NetWorks to ensure the maximum opportunities for leadership and engagement.

Dr. Levine

What do you consider to be the greatest strength of CHEST, and how will you build upon this during your Presidency?

Our greatest strengths are the education we deliver; the people at all levels who deliver, learn from, and support the delivery of this core component of our vision and mission; and the culture in which this all takes place. These people include leaders, volunteers, faculty, members and all clinicians on the health-care team, and our top-notch staff (our EVP/CEO, Executive and Operations Team and staff at all levels). To build upon this, we need to strive for continued educational innovation and relevance and creative delivery of our educational products.

What are some challenges facing CHEST, and how will you address these challenges?

Ironically, maintaining our greatest strengths in the setting of a changing health-care environment can also be one of the greatest challenges. We must continue to make our education vibrant, relevant, and experiential. To do this, we need to ensure innovative, year-round education, whether at the annual meeting or through our e-learning platforms, simulation activities, SEEK, state-of-the-art guidelines, board review courses, and courses and meetings at CHEST Global Headquarters in Glenview, Illinois, or at a global destination. We also need to stay relevant from the point of view of the value of membership and engagement. We must be cognizant of what members and others who engage with CHEST are looking for and ensure that we are meeting those ongoing expectations. Also, the need to identify, attract, develop, and retain talented and diverse members, volunteers, faculty, and future leaders and staff is imperative. As a program director, I am particularly interested in the retention of our fellows-in-training.

And finally, what is your charge to the members and new Fellows (FCCPs) of CHEST?

Get involved and stay involved. There are so many opportunities to do this! Attend the CHEST Annual Meeting. Join a NetWork. Submit articles to the journal *CHEST* or abstracts and case reports to the meeting. Participate in a Board Review Course or one of our e-learning opportunities. Come to a live course at headquarters or at a global destination. Participate in a simulation experience. Network at a meeting or a course. Engage with the CHEST Foundation. Connect with us on social media. Sign up to be a moderator and/or grader at the CHEST Annual Meeting. Become an FCCP. Apply for leadership openings, and if you don't get it the first time, try again! You will be impressed with all that CHEST has to offer!

Broad cross section of clinical topics highlights NAMDRC 2020 Conference

BY PHIL PORTE
NAMDRC Executive Director

NAMDRC will host its Annual Educational Conference at the Scottsdale Resort at McCormick Ranch in Scottsdale, Arizona, March 12-14, 2020, and features a wide cross section of clinical, management, and health policy issues.

The NAMDRC Educational Conference is unlike other medical conferences you have attended. Conference sessions begin early each day and conclude by 12:30 so attendees, spouses, and guests can enjoy the venue, this year in Scottsdale, Arizona. All registrants and their guests enjoy numerous complimentary meals, and speakers and corporate partners invariably linger with the attendees during receptions for those more casual opportunities for conversations and less formal Q&A.

The Program Committee has announced its plans to focus the first day of the 3-day event on lung cancer, severe asthma, and pulmonary hypertension. Speakers include Maxwell Smith, MD from the Mayo Clinic, Arizona; James Herman, MD, Co-Director of the Lung Cancer Program at UPMC, and Colleen Channick, MD, FCCP, Director of Interventional Pulmonary at UCLA Medical Center to address timely updates on lung cancer diagnosis and treatment. The morning sessions also include a presentation on severe asthma by Monica Kraft, MD, FCCP, University of Arizona; and Richard Channick, MD, Geffen School of Medicine, UCLA, examining pulmonary hypertension with a concentration on current

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approaches to diagnosis and treatment.

On Friday, March 13, the focus shifts from the clinical to the changing landscape in the delivery of medicine, with a concentrated focus on innovation and new tools available to guide physicians in treatment of their patients. Claibe Yarbrough, MD, National Program Director of Pulmonary, Critical Care and Sleep at the VA, University of Texas, will examine the growth of telemedicine in the ICU. Steve Peters, MD, FCCP, a past President of NAMDRC and a current Board member, will look at artificial intelligence and the future of medicine. Dr. Peters will also present a practice management update in partnership with Alan Plummer, MD, FCCP, as he addresses coding changes in the practice of pulmonary, critical care, and sleep medicine effective 2020-21.

Shifting back to a clinical focus, the Walter J. O'Donohue memorial lecture will be given by Gerald Criner, MD, FCCP, Temple University, to examine endobronchial valve therapy for emphysema. Rounding out the presentations will be luncheon speaker Susan Tanski, MD, looking at electronic nicotine delivery systems.

On Saturday, the topics turn to sleep and mechanical ventilation. Insomnia is the subject matter for Jennifer Martin, MD, Geffen School of Medicine at UCLA; Sairam Parthasarathy, MD, at the University of Arizona, will address sleep and noninvasive mechanical ventilation. And, in a corollary presentation, home mechanical ventilation is the topic for John Hansen-Flaschen, MD, FCCP, Hospital of the University of Pennsylvania.

The final morning rounds out with controversies in septic shock, Rodrigo Cartin-Ceba, MD, at the Mayo Clinic in Scottsdale, and palliative care in the ICU, Mark Edwin, also from the Mayo Clinic.

For more information about membership in NAMDRC and conference information, visit its website at www.namdrc.org.

SLEEP STRATEGIES

Noninvasive ventilation: Redefining insurance guidelines

BY ASHIMA SAHNI, MD, AND LISA WOLFE, MD, FCCP

Noninvasive ventilation (NIV) supports patient's breathing without the immediate need for tracheotomy or intubation. The Center for Medicare & Medicaid Services (CMS) defines respiratory assist devices (RAD) as bilevel devices with back-up respiratory rate capability, which provide noninvasive modes of ventilation for respiratory insufficiency or sleep-related respiratory disorders in a home or hospital setting (21 CFR 868.5895). These devices are smaller in size with provision of the external battery (if needed) but limited by inability to offer daytime ventilatory mode (ie, mouthpiece ventilation). Currently, RADs have been in DMEPOS Competitive Bidding Program since 2011 (similar to PAP devices for sleep apnea syndromes), which puts a 13-month capped rental in which the patient gets the device, supplies, and services for 13 months subsequent to which patient owns the device and supplies are paid separately by CMS (https://www.dmecompetitivebid.com/cbic/cbic.nsf/DocsCat/Home).

On the other hand, CMS defines home mechanical ventilators (HMV) as life supporting/sustaining devices for patients of all age groups used in various settings, included but not limited to home, hospital, institutional setting, transportation, or wherever portability is needed. The ventilators have increased portability due to external and internal battery, provision of mouthpiece ventilation, and at least six pressure modes and three volumes modes. Currently, the ventilators are under the frequently and substantially serviced act [42 U.S.C. § 1395m(a)(3)]. Under this act, the patient never owns the device but the device, ancillary sup-

In January 2016, CMS consolidated billing codes for ventilators, and also reduced the reimbursement amount for noninvasive pressure support ventilators.

plies, clinical support (trained respiratory therapists), and servicing of the device are included in the monthly payments, which can last indefinitely. Thus, ventilators have both higher reimbursement rates and uncapped rental periods; beneficiaries not only pay higher monthly co-payments for these devices but also pay over a longer rental period. Nonetheless, these services are vital in keeping a certain subset of patients comfortable at home and out of higher cost settings. The current populations that directly benefit from this service are patients with polio, amyotrophic lateral sclerosis, muscular dystrophies, spinal muscle atrophy, thoracic restrictive disorder, and chronic hypercapnic respiratory failure due to COPD, to name a few. Thus, HMV has been vital in "freeing" these frail and vulnerable patient populations from their hospital beds, improving the quality of life, as well as mortality.

With the advent of technologic advancements, HMV, especially the noninvasive pressure support ventilator, is now capable of doing multiple modes, including CPAP, RAD modes, and ventilator modes. This could create a potential of abuse when the durable medical equipment supplier bills CMS for the ventilator but clinically, a lower cost CPAP, auto bi-level PAP, or RAD is indicated. The 2016 report from the Office of Inspector General (OIG) noted that CMS paid 85 times more claims for noninvasive pressure support ventilators in 2015 than in 2009 (from $3.8 million to $340 million). [https://tinyurl.com/y3ckskrb]. Expenditure increased from 2014 to 2015 alone accounted for 47% of the entire $337 million increase from 2009 to 2015. But, the report could not implicate reduced prices for CPAP devices and RADs under the Competitive Bidding Program to be driving increased billing for ventilators. They did find that the diagnoses used for these claims have shifted dramatically from neuromuscular diseases to other chronic respiratory conditions.

Since then, in January 2016, CMS consolidated billing codes for ventilators and also reduced the reimbursement amount for noninvasive pressure support ventilators. After this change, between 2015 and 2016, median monthly rental rate of products decreased from $1,561 to $1,055; a reduction of 32% [https://tinyurl.com/y3ckskrb]. CMS presently is proposing to include HMV in the competitive bidding program to help with misuse and cost reduction. But the proposed addition of the home ventilators in competitive bidding risks elimination of the vital services that are so important to keep a very "vulnerable and frail" population out of higher cost facilities. Because of this, CMS would see increased costs due to frequent emergency rooms visits, frequent intubations, ICU stays, and admissions to long-term care at skilled nursing on one hand, but negatively impacting the quality of life of these patients on the other hand. This addition would have serious unintended consequences on Medicaid recipients, especially the pediatric population.

As a clinical guide, RADs are used for similar clinical conditions as HMV but are meant for less severe respiratory conditions. Ideally, getting a RAD device for a patient should be governed by the physician's clinical judgment rather than rigorous qualification criteria, nonetheless current RAD coverage policy is not only difficult but includes unnecessary qualification criteria, and as a result, pushing the patient towards more costly ventilators. Unfortunately, CMS policies have not kept up with the technological advances of noninvasive ventilation. This has led to increased costs and utilization of noninvasive ventilators. In our opinion, including noninvasive ventilators in competitive bidding to reduce cost utilization is not the solution. CMS needs to work with medical providers, beneficiaries, and various stakeholders to revise the current respiratory assist device and home mechanical ventilator guidelines in order to ensure that the appropriate patient is eligible for the correct device, without putting a very vulnerable patient population at risk.

The proposed addition of the home ventilators in competitive bidding risks elimination of the vital services that are so important to keep a very "vulnerable and frail" population out of higher cost facilities.

Dr. Sahni is Clinical Assistant Professor, Division of Pulmonary, Critical Care, and Sleep Medicine at the University of Illinois at Chicago; Dr. Wolfe is Associate Professor of Medicine (Pulmonary & Critical Care) and Neurology (Sleep Medicine), Northwestern University, Chicago, Illinois.

Dr. Mark Rosen - My mentor, my friend

BY LISA K. MOORES, MD, FCCP

By now, most of you know that the CHEST family lost one of our dearest members and leaders in early July, Past President Mark Rosen. This loss has been felt deeply by many, not only because he was taken so suddenly, but because of who Mark was and what he meant to us. We did not get the chance to say goodbye. We shared Mark's official obituary last month in *CHEST Physician.* This month, we thought it important to share something more personal.

When I think of Mark, so many words come to mind: master educator, astute and caring clinician, researcher, mentor, leader. So many qualities come to mind: generous, kind, honest, brilliant, and funny. Mark loved CHEST. He gave so much to the organization and was happy to do so. He was one of the Past Presidents who contributed even more after his presidency than during or before. Mark left an enormous footprint on our educational programs, including the annual meeting, Pulmonary Board Review, and SEEK. He was instrumental in building our international educational programs and a key player in assisting our Chinese colleagues in establishing pulmonary fellowships in their country.

When I think of my own journey with Mark, I think back to the first time I saw him. I was a senior fellow taking the Pulmonary Board Review course in Chicago. I don't remember much from that course – except for Mark's presentations. They included everything you needed to know, in a very logical outline. More importantly, he had a presence on stage that was larger than life. He made you laugh throughout the entire talk! Mark's humor was self-deprecating, and he made you feel like you had been best friends forever---even if he'd never met you. From that first encounter, he became a giant in chest medicine to me. It wasn't too many years later that, as a junior volunteer leader in the organization, I was able to finally meet Mark. He could not have been more welcoming or humble, and he instantly took on the role of mentor. I was so lucky; not only did that mentorship grow, but so did our friendship. I quickly got to the point that I looked forward to the times I would travel for CHEST events, because I knew I would see Mark. I did establish one rule, however, when we started teaching together. I refused to follow Mark in the agenda, as there was no way I could ever live up to his presentation style and humor. I didn't want to be a let down to the crowd!

Much of what I and others have accomplished with CHEST and in pulmonary medicine is directly related to the wonderful mentors we have had in the organization, and Mark was certainly one of the most prominent. He introduced me to so many additional friends and mentors. And, Mark did this for hundreds of trainees and junior faculty throughout his career. If I were to guess, I would say that this is the thing that made him most

Courtesy Dr. Lisa Moores

From a previous CHEST Challenge Championship (from left): Dr. Lisa Moores and Dr. Bill Kelly (Challenge judges) and Dr. Mark Rosen (Challenge master of ceremonies).

proud. Yes, he was an established international expert in several areas of pulmonary medicine; he held several prominent positions in academic medicine and at CHEST. But, what made him most happy was seeing his trainees and mentees succeed – you would have thought we were one of his kids (whom he was also very proud of and loved dearly). Mark was THE example of an outstanding mentor.

The memory I will carry forever of Mark, however, is when he got on stage and was the Master of Ceremonies for the CHEST Challenge Championship. He was in his element as an educator, interacting with the next generation of chest medicine physicians. He spent the entire time making the contestants, and the audience, laugh. People came to the final round to see Mark, even if they had no dog in the fight. I will always fondly recall that way he would look over at me and the other judges if he wasn't sure about a team's answer and then have an immediate witty comeback. Many of my CHEST friends have said that Mark was the Jerry Seinfeld of CHEST. I've never watched a single episode of Seinfeld, but if this description is true, I plan to!

Mark kept his sense of humor until the very end, telling me in his final days that he chose to focus on "humor markers," rather than "tumor markers" – he said that always worked out better for him! Mark, we all miss you, friend. We can't wait to share a Chopin Martini with a twist of lemon when we see you on the other side. Thank you for all you did for your family, your patients, your trainees, your colleagues, and CHEST.

CHEST 2019 Foundation opportunites abound

As we put summer in our rear-view mirror and look ahead to the switch of seasons and the vivid colors of fall and prepare to indulge and learn at CHEST 2019, it is evident change is in the air. Fall is a time of change and learning about the many opportunities the CHEST 2019 meeting offers our members, and it is also the launch of all that is changing and new for you to be a part of the CHEST Foundation.

At CHEST 2019 this year, the CHEST Foundation will be holding their 3rd Annual Women & Pulmonary Luncheon on Monday, October 21. This annual luncheon has brought over 350 attendees together to not only collaborate on patient care while focusing on gender differences but also to discuss better ways to advocate for career advancements for women pulmonologists. A new change for this year is the addition of a networking hour following the luncheon, creating an open environment to discuss empowerment, education, and resources.

The CHEST Foundation continues to help young clinicians come to the CHEST Annual Meeting. As of today, more than $250,000 has been awarded by the Foundation in travel grants and complimentary registrations to more than 125 early career clinicians. YOU can have an impact and make a change for an individual by supporting travel grants this year.

The Foundation's most noteworthy change, and one we hope all of our membership and donors will be a part of, is the launch of our new endowment in 2019/2020. The Erin Popovich Endowment will enable access to resources for patients and families, empower patients to take charge, find support groups, seek second opinions, and more, and will support research to advance patient care and improve treatment options and outcomes. This endowment will change and improve quality of life for patients and families affected by interstitial lung disease, and we encourage you to join us at the Donor Lounge during CHEST 2019 to learn more.

As you embrace the changing of the season and prepare your highlights for CHEST 2019 in NOLA, we invite you to come and discover all the changes and impact the CHEST Foundation is making and why you are so important in all we do!

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CHEST NETWORKS

Latent TB testing. High-flow nasal cannula. Statins in OSA.

Occupational and Environmental Health

New guidelines for latent TB testing in health-care personnel

Latent infection with *Mycobacterium tuberculosis* (TB) infection is of public health concern because of the lifetime risk of reactivation, a risk highest in the first 2 years after TB infection. Treatment of latent TB infection (LTBI) reduces the risk of reactivation by as much as 90%, and, thus, screening for LTBI in high-risk populations can identify patients eligible for treatment (Horsburgh & Rubin. *N Engl J Med.* 2011;364[15]:1441). The Centers for Disease Control and Prevention (CDC) previously recommended annual testing for LTBI in health-care personnel (HCP) as a high-risk group for developing LTBI (Jensen et al. *MMWR Recomm Rep.* 2005;54[No. RR-17]).

The annual national TB rate in the United States has decreased by 73% since 1991 (Stewart et al. *MMWR Morb Mortal Wkly Rep.* 2018;67[11]:317), and surveillance data show that TB incidence among HCPs does not differ significantly from the general population. The CDC thus formed the National Tuberculosis Controllers Association

Dr. Cherian

Dr. Ahasic

(NTCA)-CDC work group to revisit the recommendations for LTBI screening in HCPs. A systematic evidence review of all studies of LTBI testing in HCPs since 2005 was performed. Analysis of data from identified studies showed that less than 5% of HCPs converted from baseline negative to positive on routine annual screening.

Based on this, the CDC updated their recommendations from the 2005 guidelines: (1) Serial annual LTBI testing is no longer routinely recommended for all HCPs but may be considered for select HCPs (eg, pulmonologists, infectious disease specialists, respiratory therapists); (2) Treatment is encouraged for all HCPs with positive LTBI testing, unless medically contraindicated; (3) The recommendations for baseline LTBI and postexposure testing in all HCPs remain unchanged (Sosa et al. *MMWR Morb Mortal Wkly Rep.* 2019;68[19]:439).

Sujith Cherian, MD, FCCP
Steering Committee Member
Amy Ahasic, MD, MPH, FCCP
Chair

Respiratory Care

Aerosol drug delivery via high-flow nasal cannula

As a noninvasive, easy-to-use oxygen device, high-flow nasal cannula (HFNC) meets patients' inspiratory demands, increases functional residual capacity, and decreases the need for intubation (Rochwerg, et al. *Intensive Care Med.* 2019;45[5]:563). Using HFNC for aerosol drug delivery is an innovative approach (Ari, et al. *Pediatr Pulmonol.*

Dr. Ari

Dr. Overgoner

2011;46[8]:795), and the seven most important things about aerosol delivery via HFNC are listed below for clinicians:

1. Aerosols can be delivered via HFNC in the treatment of patients with respiratory distress through all age groups.

2. Delivery efficiency of mesh nebulizers is greater than jet nebulizers during HFNC. Unlike jet nebulizers, they do not interfere with FiO_2 and the function of HFNC by adding extra gas flow to the system.

3. Placing mesh nebulizers before the humidifier improves aerosol delivery via HFNC.

4. Higher inspiratory flow rates with HFNC decreases aerosol delivery due to increased turbulence and impactive loss of aerosols during therapy.

5. While aerosol deposition is greater with the larger prong sizes, its size should not block more than 50% of the cross-sectional area of each nostril to allow gas leakage around the cannula.

6. Although oxygen is commonly used with HFNC, administering aerosolized medications with heliox during HFNC improves lung deposition more than oxygen.

7. Training patients on the closed mouth technique and nasal breathing during therapy may improve aerosol drug delivery via HFNC.

HFNC is a promising tool in aerosol therapy, and developing clinical guidelines on aerosol delivery via HFNC is needed to improve its effectiveness in drug delivery.

Arzu Ari, PhD, RRT
Steering Committee Member
Jessica Overgoner, RRT
NetWork Member

Sleep Medicine

Statins in OSA

Obstructive sleep apnea is linked with cardiovascular disease (CVD) (Wolk R, et al. *Circulation.* 2003;108[1]:9), and the primary treatment of OSA, ie, continuous positive airway pressure (CPAP), may reverse the adverse CVD sequelae associated with OSA. However, recent randomized controlled trials, including SAVE and RICCADSA, fail to show significant reductions in CVD events with CPAP therapy (McEvoy RD, et al. *J Thorac Dis.* 2010;2[3]:138; Peker Y, et al. *Am J Respir Crit Care Med.* 2016;194[5]:613). Although numerous reasons are postulated for these unexpected trial findings, one potential explanation is that individuals in these trials were already on CVD protective drugs. One such drug category is statins. Statins are prescribed for their lipid lowering effects; however, they have pleiotropic properties including reduction in vascular inflammation and oxidative stress. Statins also enhance endothelial function and improve blood pressure. In animal studies, statins prevented the adverse effects of chronic intermittent hypoxemia on systolic blood pressure, endothelial function, and carotid artery

compliance. Human studies confirm some of the aforementioned animal study findings. In a study of patients with OSA, statin therapy preserved the anti-inflammatory cell surface proteins that are typically reduced in these patients (Emin M, et al. *Sci Transl Med.* 2016;8[320]:320ra1). In a randomized controlled trial of patients with OSA, statin therapy significantly improved systolic blood pressure but did not improve reactive hyperemia index, which is a marker of endothelial dysfunction (Joyeux-Faure M, et al. *Mediators Inflamm.* 2014 Aug 25. doi: 10.1155/2014/423120).


Dr. Shah

Therefore, the jury is still out regarding the independent impact of statin therapy on CVD risk reduction in patients with OSA. Yet, there is select evidence suggesting there may be a role for statins in patients with OSA to mitigate the CVD risk associated with OSA. It remains unknown whether statins work synergistically with CPAP to further reduce CVD risk.

Neomi Shah, MD
Steering Committee Member

CHEST Annual Meeting 2019 introduces Wellness Zone with tips and tricks to manage stress

Working as a clinician doesn't always allow for extra time to focus on the wellness of your body and mind. After taking care of patients all day, it's important to find the time to also take care of yourself.

This year's CHEST Annual Meeting is introducing a new interactive experience that aims to provide physicians with the necessary tools to decompress from the stressors of work. Visit the CHEST Wellness Zone to learn easy methods to handle stress and relax after a long day at work.

CHEST 2019 attendees will learn tips and tricks geared toward improving health, and consultants will provide attendees with personalized methods to maintain a healthy lifestyle in the workplace and at home. For those who have yet to register for the annual meeting, this new initiative, along with the wealth of education opportunities, might change your mind.

At the Wellness Zone, you can relax while getting your feet massaged at one of the four massage machine stations. Clinicians are always on the go, and this station will help to relieve the pressures of being on your feet all day at work.

Essential oils will also be on display for you to smell. Experts will show you the best oil combinations to use in and out of the office.

With a daily strenuous workload, clinicians often forget about their own health, which can lead to poor posture. The Wellness Zone is equipped with consultants who will examine your posture to provide you with feedback to improve your stance. You will walk away after an evaluation with before and after pictures from your consult and a full posture analysis report.

Do you want to try meditation? There is a space dedicated to guiding you through a first-time practice equipped with headphones. You can visit this area to learn about guided meditation apps that make it easy to follow along when meditating at work and home.

The Wellness Zone will feature a variety of 15- to 30-minute sessions focused on providing you with the resources to create a new wellness routine after the annual meeting's conclusion.

Geared toward improving both one's physical and mental health, these sessions will dive deeper into maintaining a healthy lifestyle while at work and home. You will walk away from the Wellness Zone with new habits that you are encouraged to incorporate into your daily life to keep your stress levels down to avoid burnout.

The Wellness Zone will be located in the lobby/foyer space inside the New Orleans Ernest N. Morial Convention Center and will be open all day October 20-23, except during the Opening Sessions. Attendees can visit the Wellness Zone at any time with no appointment necessary.

Visit chestmeeting.chestnet.org for a list of sessions that are offered in the Wellness Zone, including Creating Well-Being in the Workplace and more. Plan your visit now to enjoy all the benefits CHEST 2019 has to offer.

CHEST 2019 introduces self-study bundles for additional CME/MOC

This year, in conjunction with CHEST 2019, CHEST is piloting self-study bundles that will allow attendees to earn additional Continuing Medical Education/Continuing Education credits and American Board of Internal Medicine Maintenance of Certification points, apart from the total credits available for the overall meeting. Attendees will receive complimentary access to the eight self-study bundles, in which they will read articles and answer questions related to the articles, in the following areas:

- Pulmonary Hypertension
- Critical Care
- Sleep
- COPD
- Asthma
- Lung Cancer
- Interstitial Lung Disease
- Transplant

This value-added addition will offer the opportunity to earn three credits CME/CE and the corresponding number of ABIM MOC points for each bundle; if someone completes all eight bundles, they can earn up to 24 credits.

The deadline for completion of and claiming CME/CE for the self-study bundles is the same as the claiming deadline for the CHEST Annual Meeting, February 29, 2020.

This month in the journal *CHEST*®

Editor's picks

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

COMMENTARY

Rare Lung Disease Research: National Heart, Lung, and Blood Institute's Commitment to Partnership and Progress.
By Dr. L. J. Vuga, et al.

ORIGINAL RESEARCH

Validation of Predictive Metabolic Syndrome Biomarkers of World Trade Center Lung Injury: A 16-Year Longitudinal Study.
By Dr. S. Kwon, et al.

Association of Short Sleep Duration and Atrial Fibrillation.
By Dr. M. W. Genuardi, et al.

Determinants of Depressive Symptoms at 1 Year Following ICU Discharge in Survivors of 7 or More Days of Mechanical Ventilation: Results From the RECOVER Program, a Secondary Analysis of a Prospective Multicenter Cohort Study.
By Dr. M. Hamilton, et al.

TOPICS IN PRACTICE MANAGEMENT

Clinician Strategies to Improve the Care of Patients Using Supplemental Oxygen.
By Dr. S. S. Jacobs

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