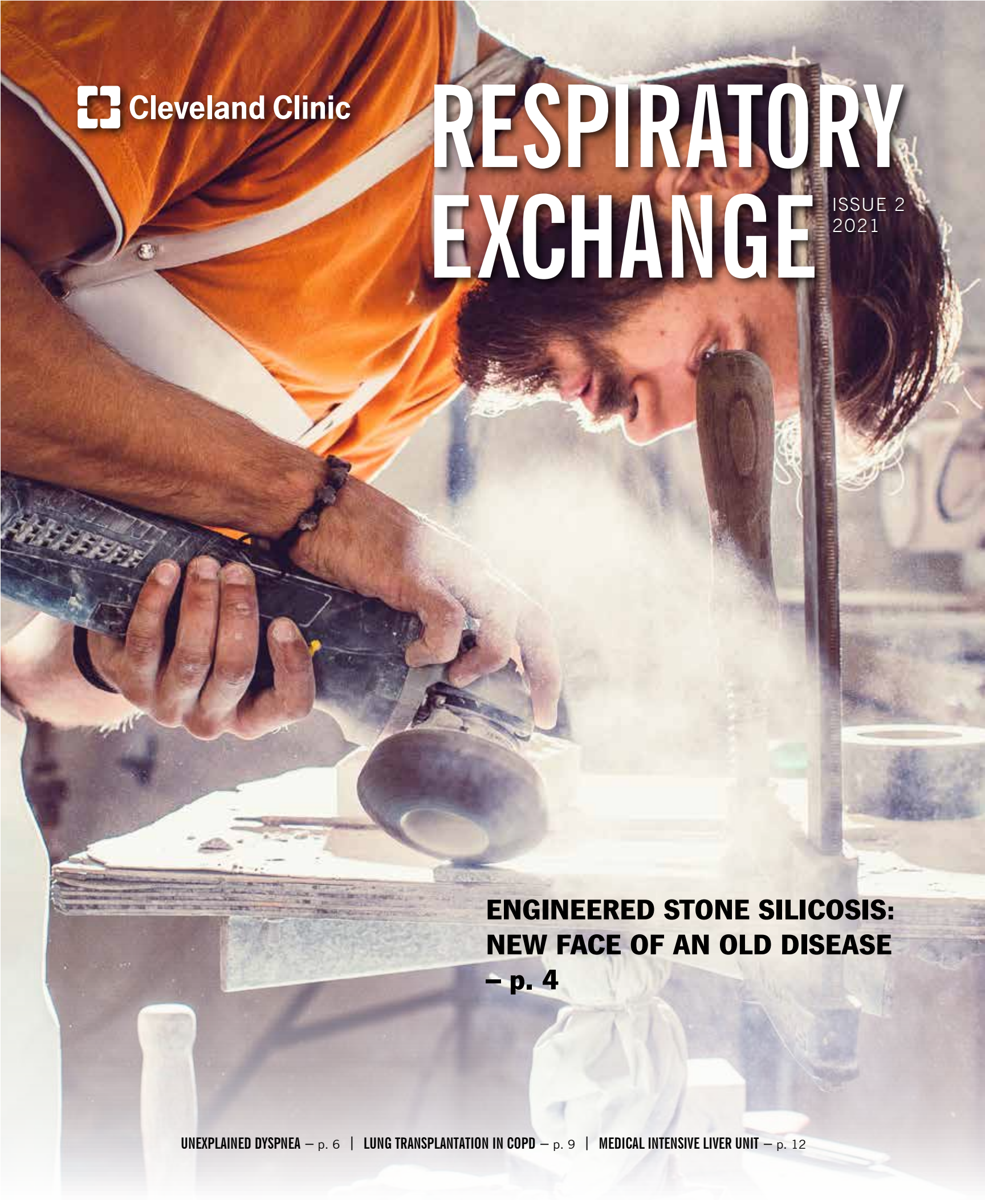


Cleveland Clinic

RESPIRATORY EXCHANGE

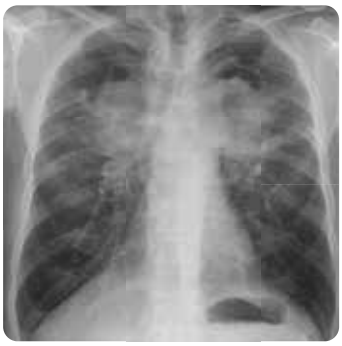
ISSUE 2
2021

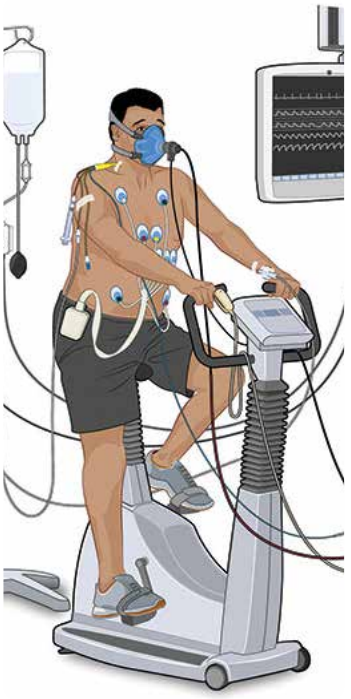
ENGINEERED STONE SILICOSIS: NEW FACE OF AN OLD DISEASE

– p. 4

At the Respiratory Institute, specialists in pulmonology, allergy and immunology, infectious disease, and critical care medicine work in close collaboration to diagnose and manage the full spectrum of pulmonary and allergic disorders, serving more than 200,000 patients annually. The institute is part of Cleveland Clinic, a nonprofit, multispecialty academic medical center integrating outpatient and hospital care with research and education for better patient outcomes and experience. More than 4,500 staff physicians and researchers provide services through 20 patient-centered institutes. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*.

INSIDE





DEAR COLLEAGUES,

RAED DWEIK, MD, MBA
Chairman, Cleveland Clinic
Respiratory Institute

Coal workers' pneumoconiosis (black lung disease) and chronic beryllium disease may seem like medical history — diseases of the past. But occupational lung diseases like these certainly have not been eradicated. In fact, today new lung diseases are being brought on by new types of occupational exposure. Engineered stone silicosis, featured on the cover of this issue of *Respiratory Exchange*, is one example of a disease that has been increasing in prevalence since it was first identified in 2012.

The accompanying article on page 4 is written by one of our newest staff members in Cleveland Clinic's Respiratory Institute. Maeve MacMurdo, MD, joined us in July after completing a fellowship in pulmonary and critical care medicine here at Cleveland Clinic. Her specialty focus on occupational lung disease, including research on novel exposures, adds new expertise to our team. Dr. MacMurdo has established Cleveland Clinic's Occupational Lung Disease Clinic, with several locations throughout Ohio, all with direct access to our diffuse parenchymal lung disease, lung transplant and other leading programs.

This issue of *Respiratory Exchange* also features other Respiratory Institute experts with fresh, new insights on:

- Unexplained dyspnea — shedding light on chronically low preload state.
- When to consider lung transplantation for patients with chronic obstructive pulmonary disease (COPD).
- Using virtual technology to manage critically ill patients — something we expanded in our Medical Intensive Liver Unit during the COVID-19 pandemic.
- Increasing accessibility to transplantation for patients with HIV.
- The effect of alcohol use disorder in patients with asthma or COPD.

I hope these articles will inspire you to consider new approaches as you care for your patients of today. Please also see the expanded list of clinical studies near the end of this publication, and consider offering your patients the opportunity to participate in our research as we prepare to care for the patients of tomorrow.

Thank you for your interest in our program.

Sincerely,

RAED DWEIK, MD, MBA
Chairman, Cleveland Clinic Respiratory Institute | E. Tom and Erika Meyer Chair in Pulmonary Medicine

ENGINEERED STONE SILICOSIS: NEW FACE OF AN OLD DISEASE

By Maeve MacMurdo, MD

KEY POINTS

Since late 2019, multiple cases of severe silicosis have been identified in fabricators of engineered stone (quartz) kitchen countertops.

"Simple" chronic silicosis is characterized by small (less than 1 cm) nodules, predominantly in the upper lobe. Patients endorse progressive dyspnea and cough. Over time nodules may coalesce, resulting in fibrotic lung disease.

Options for treatment are extremely limited.

Avoiding dry cutting, using engineering controls and wearing personal protective equipment can help prevent silicosis.

A thorough occupational history should be part of any evaluation for interstitial lung disease.

Employment in kitchen construction may not raise red flags during the assessment of a patient with unexplained dyspnea. However, since late 2019, multiple cases of severe silicosis have been identified in fabricators of engineered stone kitchen countertops across the United States, Australia, Israel and Europe.[1,2]

The rise and the risk

Engineered stone (also known as quartz) is an alternative to traditional marble products and is increasingly utilized in home renovation and commercial construction. Made by mixing quartz crystals with a resin binding product, engineered stone may be comprised of as much as 90% silica, significantly higher than other materials such as granite or sandstone.[3] As a result, cutting, grinding and polishing engineered stone products without appropriate engineering controls can result in significant release of respirable crystalline silica (RCS) — placing exposed workers at increased risk for the development of silicosis.

The risk of silicosis associated with engineered stone fabrication was first identified in 2012, after an outbreak of severe silicosis was seen in Israeli workers who had dry-cut engineered stone products.[4] Investigation of 800 workers in Australia has revealed more than 160 cases of silicosis among engineered stone fabricators, and case finding continues.[1,5] In the United States, multiple clusters of silicosis have been identified among engineered stone fabricators, the majority of whom had late-stage disease at the time of diagnosis.[2]

While medical surveillance for silicosis is mandated for at-risk workers by the Occupational Safety and Health Administration (OSHA) 2018 final ruling on RCS, rates of screening uptake remain low, with less than 11% of employers in one state offering routine medical surveillance.[6] The vast majority of engineered stone fabrication operations are small businesses with fewer than 10 employees. These employers often face additional barriers to instituting medical surveillance.[7] Consequently, it is likely that many patients with silicosis related to engineered stone fabrication remain unrecognized.

Clinical manifestations

Classically, silicosis presents along a spectrum of disease severity. The risk of developing silicosis is related to the duration and intensity of exposure.

"Simple" chronic silicosis is characterized by the development of small (less than 1 cm), upper-lobe-predominant nodules, which may be accompanied by hilar lymphadenopathy. Patients endorse progressive dyspnea and cough and may show evidence of restrictive, obstructive or mixed deficits on pulmonary function testing. Over time these nodules may coalesce, resulting in fibrotic lung disease and significant symptom burden.

Accelerated silicosis is characterized by a more rapid progression to severe fibrotic lung disease, also known as "progressive massive fibrosis" (Figures 1 and 2). The majority of engineered stone workers diagnosed with silicosis have presented with this accelerated form, reflecting a pattern of high-intensity exposure to RCS.[2,4,8] Due to the high levels of RCS exposure, these workers may experience progression of the disease even after exposure cessation.[9]

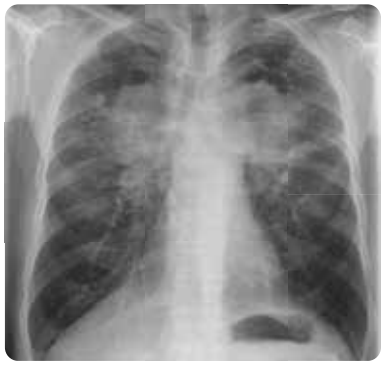
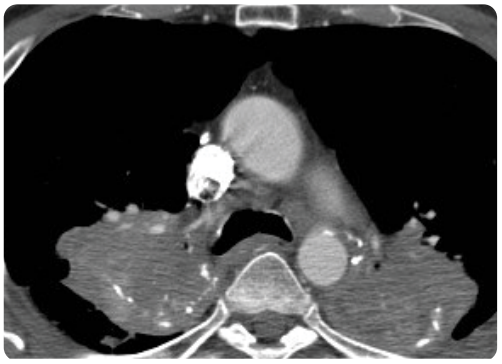


FIGURE 1. Chest X-ray highlighting the upper-lobe-predominant bilateral opacifications classic in progressive massive fibrosis.



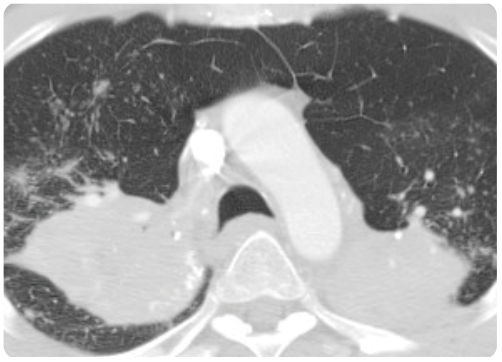


FIGURE 2. Chest CT showing large masslike conglomerates consistent with progressive massive fibrosis.

Options for treatment are limited

Once silicosis has developed, options for treatment are extremely limited. Removal from further exposure to RCS may reduce the risk and speed of disease progression. Other therapies, including whole lung lavage (a procedure in which large volumes of saline are flushed into the lungs and then removed), have been trialed. However, outcomes are mixed, particularly in patients whose disease already has progressed to the point of fibrosis. Transplantation is an option, and referral to a specialized transplantation center should be considered early in patients with accelerated silicosis.

Reducing occupational exposures to prevent silicosis

Silicosis is preventable. Through avoidance of dry cutting, utilizing engineering controls to reduce dust release and improve ventilation, and providing appropriate personal protective equipment in situations where dry cutting cannot be avoided, the amount of RCS a worker is exposed to can be significantly reduced. We are working to better understand silicosis prevention practices among employers in the engineered stone fabrication field and to develop targeted resources to help reduce RCS exposure.

For employers who want to develop or strengthen their own silicosis prevention practices, Cleveland Clinic's occupational lung disease team and the Cleveland Clinic AtWork® employee health program can provide expert guidance and resources to help develop medical surveillance programs and keep workers safe.

While occupational lung diseases such as silicosis may seem like diseases of history, new occupational exposures associated with an increased risk of silicosis continue to be identified. A thorough occupational history should form part of any diagnostic evaluation for interstitial lung disease.

For more information on Cleveland Clinic's Occupational Lung Disease Clinic, call 216.445.4538.

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Dr. MacMurdo recently completed Cleveland Clinic's Pulmonary & Critical Care Medicine Fellowship Program. She now is staff in the Respiratory Institute, where her practice includes treating patients with occupational lung diseases. She can be reached at macmurm@ccf.org or 216.444.4707.

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UNEXPLAINED DYSPNEA: COULD IT BE DUE TO A CHRONICALLY LOW PRELOAD STATE?

By Adriano Tonelli, MD

KEY POINTS

Unexplained dyspnea may be due to a chronically low preload state. Insufficient venous return can result in inadequate cardiac output and symptoms such as dyspnea, particularly when standing or during exercise.

The mainstay of diagnosis is invasive cardiopulmonary exercise testing.

Treatment requires a holistic approach, including pharmacological and nonpharmacological interventions (e.g., increased hydration, use of compression stockings, exercise training).

Dyspnea is a common complaint faced by primary care physicians, cardiologists and pulmonologists in the outpatient clinic. After a comprehensive diagnostic evaluation, the cause of dyspnea may remain elusive in 10%-20% of patients.

A chronically low preload state may be responsible for the dyspnea in several of these patients.[1] In a chronically low preload state, there is insufficient venous return, which results in inadequate cardiac output and the development of symptoms such as dyspnea, particularly when standing or during exercise. The exact mechanism of dyspnea remains obscure, but plausible explanations include ventilation/perfusion mismatch, respiratory muscle fatigue, skeletal muscle dysfunction, deconditioning, and imbalance between respiratory neural drives and afferent feedback of the respiratory system.

Making a diagnosis

Conditions associated with chronically low preload states can be broadly categorized in three groups: a decrease in intravascular volume, venous obstruction/restriction and reduction in venous tone. Increased venous capacitance and excessive blood pooling in the lower extremities are seen in patients with postural orthostatic tachycardia syndrome (POTS), orthostatic hypotension and small fiber neuropathy. The diagnosis of a chronically low preload state as the reason for dyspnea involves a focused clinical history, including an evaluation of the autonomic system, determination of orthostatic vital signs, and tests to assess the cardiovascular, neurological and autonomic functions. Importantly, the mainstay of diagnosis is invasive cardiopulmonary exercise testing (iCPET) (Figure).

Preload is defined as the force to stretch fibers at the end of diastole and depends on several factors, such as ventricular dimension and compliance, wall thickness, transmural diastolic pressure, ventricular interdependence and venous return. When standing, there is a shift of 700-900 mL of blood volume to the lower body that is counterbalanced by a reduction in venous compliance in combination with functional venous valves, muscle contraction and the suctioning action of the respiratory pump. The measurement of preload in vivo is challenging but can be estimated by the right atrial and pulmonary artery wedge pressure obtained during right heart catheterization.

The iCPET collects information traditionally provided by cardiopulmonary exercise testing but adds simultaneous hemodynamic and gasometric information from pulmonary and radial artery catheterization. Therefore, the iCPET provides a comprehensive evaluation of ventilation, gas exchange and cardiac function at rest and during incremental exercise. There is no consensus regarding the hemodynamic definition of preload insufficiency, but the condition needs to be considered in cases of an unexplained abnormal cardiac limitation to exercise (peak oxygen consumption $<$ 80% of predicted and peak cardiac output $<$ 80% of predicted), combined with reduced ventricular preload (peak right atrial pressure $<$ 9 mm Hg, peak pulmonary artery

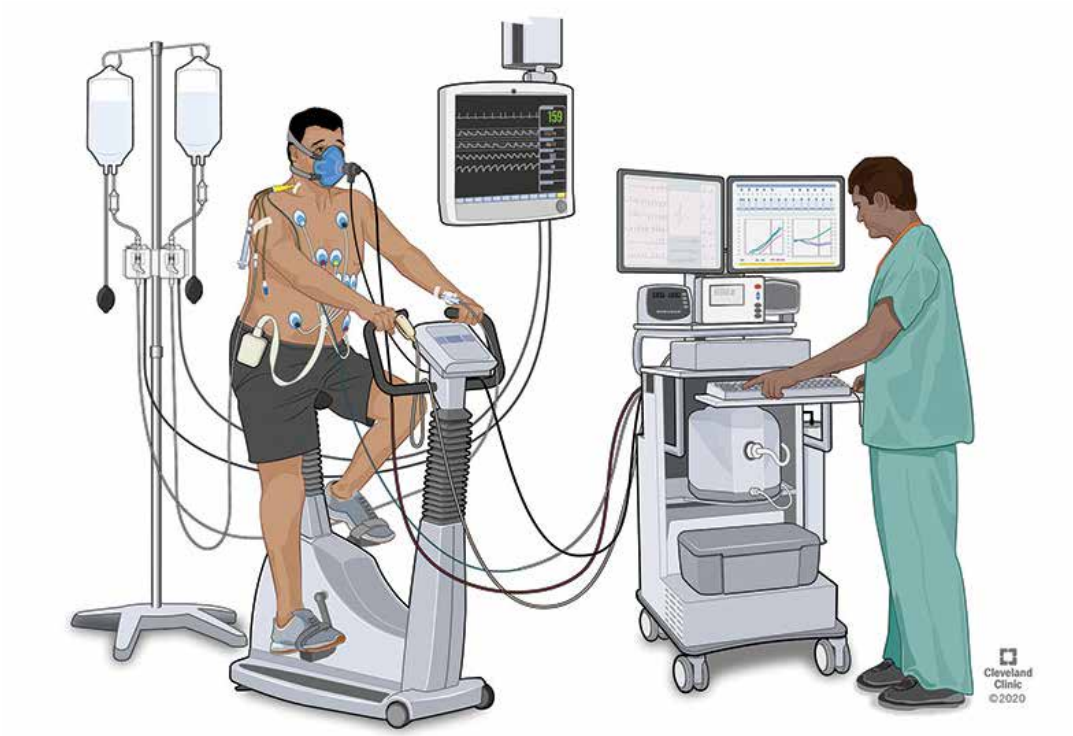

FIGURE. Invasive cardiopulmonary exercise is the gold-standard test for diagnosing a chronically low preload state as the reason for dyspnea. Additionally, a focused clinical history, including an evaluation of the autonomic system, determination of orthostatic vital signs, and tests to assess the cardiovascular, neurological and autonomic functions, should be obtained.

wedge pressure < 14 mm Hg and peak pulmonary artery pressure < 30 mm Hg).

Managing the condition holistically

The management of a chronically low preload state requires a multidisciplinary team, including pulmonologists, cardiologists, neurologists, rheumatologists, exercise physiologists and other professionals. The goal is to diagnose the condition, identify the cause of the chronically low preload state and provide the best treatment.

Treatment requires a holistic approach, including pharmacological and nonpharmacological interventions. We aim to optimize the volume status by increasing hydration and salt intake, and using over-the-knee or, ideally, waist-high compression stockings. Another critical component is exercise training, with endurance and resistance training focused on the core and lower body.

When nonpharmacologic measures are insufficient, we use medications such as salt tablets and fludrocortisone to increase blood volume, midodrine to increase sympathetic activity, pyridostigmine to increase peripheral cholinesterase, and other interventions. In certain inflammatory/autoimmune conditions, we consider intravenous immunoglobulin, rituximab or other agents.

In summary, a chronically low preload state should be considered in patients with unexplained dyspnea. The specific cause needs to be investigated by a multidisciplinary team to deliver the best treatment strategy.

Dr. Tonelli is staff in the departments of Pulmonary Medicine, Critical Care Medicine and Pathobiology. He can be reached at tonella@ccf.org or 216.444.0812.

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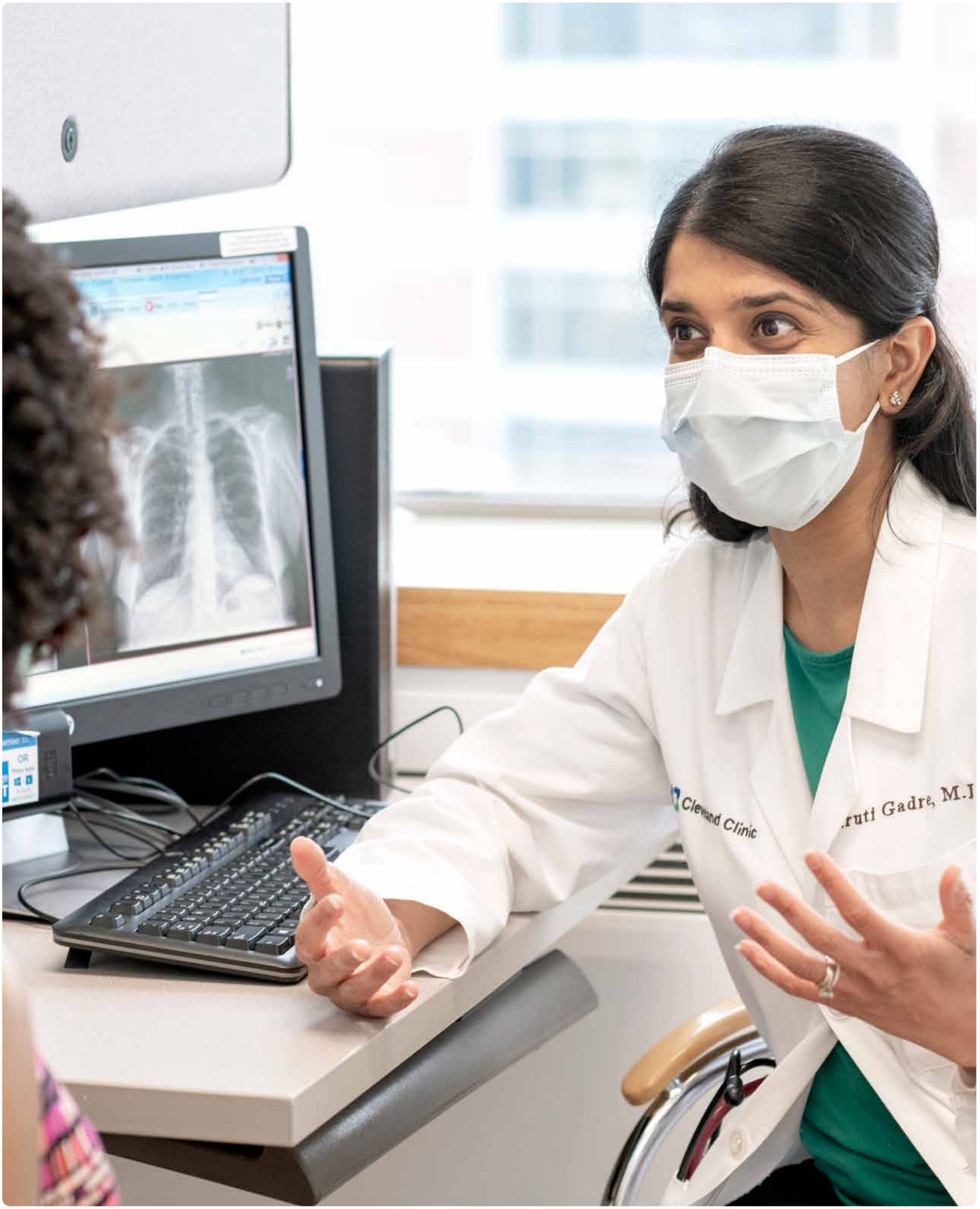
Cleveland Clinic

WHEN IS LUNG TRANSPLANTATION AN OPTION IN COPD?

By Shruti Gadre, MD

KEY POINTS

Because of the slow progression of COPD, determining a survival benefit from lung transplant can be challenging.

Patients with COPD typically are listed for transplant when they meet at least one of the following criteria: BODE index ≥ 7, FEV_1 < 15% to 20% predicted, three or more severe exacerbations during the preceding year, one severe exacerbation with acute hypercapneic respiratory failure, or moderate to severe pulmonary hypertension.

When a patient doesn't yet qualify to be listed, consider management strategies such as pulmonary rehabilitation and lung volume reduction.

Early referral to a transplant center is always beneficial.

Patients with chronic obstructive pulmonary disease (COPD) are one of the largest cohorts referred for lung transplantation. However, the criteria for referral and the indications for transplant aren't always clear.

Regardless, early referral to a transplant center is always beneficial, even if the patient is not yet deemed to be a transplant candidate.

COPD versus other end-stage lung diseases

COPD is the third leading cause of death globally and remains the most common reason for lung transplantation worldwide. Patients with COPD and alpha-1 antitrypsin deficiency (AATD) accounted for 34.7% of all lung transplants performed between 1995 and 2018, according to an International Thoracic Organ Transplant Registry report.[1]

It is important to note several key differences between COPD and other end-stage lung diseases that merit referral for lung transplant. Patients with COPD:

- Experience a loss in lung function over a longer period of time. It can become difficult to determine when in the course of the disease patients should be referred or listed for transplant. The long natural history means that these patients have the potential for more deconditioning. Waiting too long to transplant allows for progression of debility.
- Have less short-term mortality. Even in advanced stages of COPD, short- and intermediate-term survival is better than in other diseases for which lung transplant is performed. Because mortality in COPD is seen beyond one year, patients with COPD receive a lower lung allocation score (LAS), are prioritized lower on the transplant waitlist and thus have longer wait times.
- Experience a progressive decline in quality of life. There is debate on whether quality of life should be considered when making decisions about lung transplantation. Currently, the LAS does not factor in a quality-of-life benefit. Therefore, patients with COPD may be disadvantaged.
- Have a longer lung transplant window. The window for lung transplantation is the period of time when the disease is advanced enough for the patient to benefit from a transplant without being too ill to undergo the operation. When a patient is within that window, the benefits of transplant outweigh the risks, and the patient should be listed for transplantation. It is best to refer a patient earlier in the transplant window or before it. An early referral allows the transplant pulmonologist and referring physician time to collaborate and optimize the patient for transplant by enrolling them in pulmonary rehabilitation, weaning maintenance systemic steroids, evaluating and treating obstructive sleep apnea, and working on weight loss.

Determining survival benefit

The median survival after lung transplantation is 6.7 years. Even for patients with advanced COPD, this time may be shorter than the expected survival without transplant. Because of the slow progression of COPD, a survival benefit from transplant is not always easy to discern.

LEFT: Lung transplant physician Shruti Gadre, MD, explains that because of the slow progression of COPD, a survival benefit from transplant is not always easy to discern.

To identify patients most likely to benefit from transplant, we must consider:

- Predicted mortality. Low forced expiratory volume in one second (FEV_1) is the most common reason for referral to a lung transplant center, but by itself it is insufficient to determine benefit from transplantation. The BODE index — which combines body mass index (BMI), FEV_1, Modified Medical Research Council dyspnea score and 6-minute walk distance (6MWD) into weighted scores on a 10-point scale — has proved to be a better indicator of survival than the spirometric staging system alone. A BODE score of 7-10 is associated with a mortality rate of 80% at four years; a score of 5-6 is associated with a mortality rate of 60% at four years. Thus, patients with a BODE score of 7 or higher may be appropriate for transplant.[2]
- Predicted survival after lung transplant. Further complicating patient selection, several factors that predict higher mortality in COPD also are associated with poor outcomes after transplant.[3] For example, physical deconditioning can lead to reduced 6MWD and predispose the patient to worse outcomes after transplant. Low BMI and older age are associated with shorter survival after transplant. Pulmonary hypertension increases the relative risk of mortality at one year after transplant in patients with COPD compared to patients with idiopathic pulmonary fibrosis or cystic fibrosis.
- Quality of life. Literature on the impact of lung transplant on quality of life for patients with COPD is limited. However, a 2011 study reported that patients with a BODE score of 5-6 had similar improvements in quality of life after transplant as patients with a BODE score of 7-10, indicating that transplant can improve quality of life even when it is not expected to have a mortality benefit.[4]

Therefore, it is challenging to identify patients with advanced COPD who will achieve both a survival and quality-of-life benefit from a lung transplant. Determining a patient's suitability for transplant is a complex decision made by engaging the expertise of multidisciplinary teams and considering the best available data. Decisions are made on a case-by-case basis, but patients typically are listed for transplant when they meet at least one of the following criteria:

- BODE index ≥ 7.
- $FEV_1 < 15\%$ to 20% predicted.
- Three or more severe exacerbations during the preceding year.
- One severe exacerbation with acute hypercapneic respiratory failure.
- Moderate to severe pulmonary hypertension.[5]

Management strategies for patients without survival benefit

When a patient doesn't (or doesn't yet) qualify to be listed for transplant, there are several management strategies to consider:

- Referral to a transplant center. Patients may eventually progress into the transplant window.

"... early referral to a transplant center is always beneficial, even if the patient is not yet deemed to be a transplant candidate."

- Pulmonary rehabilitation. This provides well-established benefits in COPD for dyspnea, exercise capacity and health-related quality of life. Pulmonary rehabilitation is also required for lung transplant candidates. Patients unable to participate are unlikely to be candidates for transplant.
- Lung volume reduction (surgical or endobronchial). Some patients may be candidates for this procedure, either instead of or as a precursor to lung transplant. Successful lung volume reduction, and the associated improvement in functional and nutritional status, can improve a patient's suitability for transplant.

Previous cardiothoracic surgery and endoscopic or surgical lung-volume reduction are not contraindications to lung transplantation.

In summary, not all patients with COPD will derive a mortality benefit from transplant. Identifying those who are likely to benefit can be challenging. Management strategies are available for patients who do not yet but may ultimately have a survival benefit. Early referral to a transplant center is beneficial because it allows the opportunity to optimize a patient's condition to make the patient a better candidate for lung transplant.

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Dr. Gadre is a lung transplant physician and critical care specialist. She can be reached at gadres@ccf.org or 216.444.0655.

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OPERATING A MEDICAL INTENSIVE LIVER UNIT DURING A PANDEMIC

KEY POINTS

Patients with advanced liver disease admitted to Cleveland Clinic's Medical Intensive Liver Unit (MILU) have a higher transplant-free survival rate than those not in the MILU.

During the COVID-19 pandemic, patients presented sicker — including with complications related to COVID-19.

During the pandemic, the MILU team used virtual technology to stay connected, closely monitoring and co-managing patients, continuing the transplant workup and optimizing patients for surgery.

Although the number of patients cared for in the MILU was down from 436 in 2018-2019 to 373 in 2020, the transplant team performed more transplants than ever before in 2020.

When clinicians across medical disciplines at Cleveland Clinic joined forces in 2018 to establish an evidence-based intensive care unit for patients with advanced liver disease, they built daily, in-person multidisciplinary collaborations into the model. Patients were triaged into a single geographical unit staffed by nurses trained in liver-specific protocols.

Their planning paid off, according to data shared during Digestive Disease Week in 2019. Patients admitted to the Medical Intensive Liver Unit (MILU) experienced a higher transplant-free survival rate (79.5%) compared with a survival rate of 70.8% among patients in the non-MILU group ($P = 0.015$).

"We were encouraged by our successes while continuously fine-tuning our processes and caring for the sickest patients," says Aanchal Kapoor, MD, staff in the Department of Critical Care Medicine and Director of the MILU. "And then COVID-19 hit. Our space was needed for these very infectious patients, our highly trained staff were diverted and our core approach — frequent face-to-face collaboration among providers — was suddenly unsafe."

Downstream effects

As cases of COVID-19 surged, Christina Lindenmeyer, MD, co-Director of the MILU and staff in the Department of Gastroenterology and Hepatology, and her team quickly trained a new nursing team and adapted to a new space. But patients were presenting sicker, including those with complications related to COVID-19, and throughput was an even greater challenge given COVID-19 transfer protocols.

"Most fields saw an increase in case severity as a result of patients' reluctance to put themselves at risk during a pandemic," says Dr. Lindenmeyer. "But with liver transplantation candidates, one or two days can make the difference between staying active on the waitlist and becoming too sick to tolerate the procedure."

Nationally, hospitals saw an increase in the severity of illness for hospitalized hepatology patients over the course of the pandemic. Model for End-Stage Liver Disease (MELD) scores of patients admitted to Cleveland Clinic's MILU averaged 27.2 in the first year of operation (2018-2019). That rose to 30.1 in 2020. Although the number of patients cared for in the MILU was down from 436 in 2018-2019 to 373 in 2020, the transplant team performed more transplants than ever before in 2020.

"Over two-thirds of the patients who were admitted to the MILU in 2020 and who were eventually transplanted were able to be transplanted directly from the MILU, compared with just over one-third of MILU patients transplanted in the prior year," says Dr. Kapoor. "So, although COVID-19 interrupted or altered most of our processes, we see evidence of faster transplant evaluations, enhanced multidisciplinary collaboration and communication, and continuous improvement of our protocols. We are working harder to find pathways to safely transplant patients with critical care needs."

Another impact of the pandemic? "Our number of patients presenting with alcohol-related liver disease rose by almost 10%," says Dr. Lindenmeyer.

BELOW: Aanchal Kapoor, MD, Director of Cleveland Clinic's Medical Intensive Liver Unit, says the COVID-19 pandemic pushed her team to work harder to find ways to safely transplant patients with critical care needs.

Critical care collaboration goes virtual

The initial success of the MILU depended in large part on continuous communication among all providers: hepatologists, critical care physicians, infectious disease specialists, surgeons, nephrologists, neurologists, social workers, nurses, dietitians and pharmacists.

"We tried our best to mimic that hallway conversation, which can be so critical to what we do, in a COVID-safe way," says Dr. Lindenmeyer. "We standardized and expanded our morning huddle, implemented breakout panels for subspecialty teams and transitioned to virtual co-rounding. We utilized iPads dedicated to bringing colleagues along on the rounds virtually, and we continued our working groups to revise guidelines on indications for initiation of dialysis, nutrition optimization, antibiotic choices in the setting of sepsis and advances in the care of patients with acute liver failure."

MILU patients in 2020 had a higher Acute Physiology and Chronic Health Evaluation (APACHE) score as compared to previous years.

"This patient population offers a complex hemodynamic challenge, and decisions about transplant have to be made in a very narrow window," says Dr. Kapoor. "We leveraged virtual technology to stay connected, closely monitoring and co-managing these patients, continuing the transplant workup and optimizing patients for surgery. It was amazing to see patients with MELDs in the high 30s get transplanted within 48 hours."

The future of the MILU

The working groups formed to increase collaboration while decreasing physical contact have become a critical part of MILU infrastructure. The teams reassessed all prior unit protocols and are now working on standardizing them. The unit also recently acquired a Molecular Adsorbent Recirculating System (MARS®) to enhance the albumin dialysis and plasmapheresis programs.

The team is also reaching beyond the unit, applying their knowledge to the development of standard criteria for transplantation.

"Right now, we have limited evidence to guide us when a patient is too sick to be a viable candidate for transplant," says Dr. Lindenmeyer. "But we've built a successful unit based on protocols developed by a carefully crafted multidisciplinary team, and we plan to host an international symposium in 2022 to share that knowledge."

The MILU is also maintaining a prospective registry of patients to study outcomes and develop novel research protocols that could potentially revolutionize the care of critically ill patients with liver disease.

"It took a long time to get us to this point," adds Dr. Lindenmeyer. "But with constant reassessment, we've all found common ground in the best interest of our patients."

To arrange a patient transfer, call 216.444.8302 or 800.553.5056.

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Aanchal Kapoor, MD, is staff in the Department of Critical Care Medicine and Director of Cleveland Clinic's Medical Intensive Liver Unit (MILU). She can be reached at kapoora@ccf.org or 216.444.4100. Christina Lindenmeyer, MD, is co-Director of the MILU and staff in the Department of Gastroenterology and Hepatology. She can be reached at lindenc@ccf.org or 216.444.1108.

EXPANDING TRANSPLANTATION OPTIONS FOR PATIENTS WITH HIV

KEY POINTS

Cleveland Clinic's Transplant Center soon will begin offering kidney transplantation from deceased donors with HIV to patients with end-stage kidney disease and HIV.

The HIV Organ Policy Equity (HOPE) Act was passed in 2013 to make transplantation more accessible to patients with HIV.

Donor strains of HIV can be manageable post-transplantation, even if acquired from donors with high viral loads.

Patients can reduce their wait times for kidney transplantation by being on the list for HIV-positive donor organs in addition to remaining on the waitlist for HIV-negative donor organs.

Cleveland Clinic's Transplant Center soon will begin offering kidney transplantation from deceased donors with HIV to patients with end-stage kidney disease and HIV. The program is part of a national effort to make transplantation more accessible to patients with HIV, who face numerous healthcare disparities, according to Anita Modi, MD, associate staff in the Department of Infectious Disease in Cleveland Clinic's Respiratory Institute.

"In the 1980s, the National Organ Transplant Act was passed to prevent people with HIV from donating organs," says Dr. Modi. "At the time, HIV was devastating, and we wanted to avoid inadvertent transmission to HIV-negative transplant candidates. Now, thankfully, effective medications make HIV a chronic disease rather than a death sentence, so it has become safer to offer eligible HIV-positive transplant candidates the same lifesaving therapy we would offer HIV-negative transplant candidates with kidney disease."

Dr. Modi says that even donor viral load is not necessarily a concern for organ suitability.

"Data from other institutions show that donor strains of HIV can be manageable post-transplantation, even if acquired from donors with high viral loads," she says. "In fact, many HIV-positive organs come from donors who were unaware of their diagnosis and not on therapy prior to donation. However, antiretroviral therapy is so effective now that we can most likely devise suitable regimens for transplant recipients, regardless of donor viral load."

HOPE Act transplantations

Passed in 2013, the HIV Organ Policy Equity (HOPE) Act reversed the previous law, opening a large donor pool only available to HIV-positive transplant candidates.

"For every one person who undergoes kidney transplant, three more remain on the waitlist," says Dr. Modi. "This program makes transplantation much more likely for our transplant-eligible patients with HIV."

Per the HOPE Act, each program must be conducted under research protocol, with local IRB approval, a data safety monitoring board, and mandatory reporting of outcomes and adverse events to the United Network of Organ Sharing and the Organ Procurement and Transplantation Network. Cleveland Clinic's team created a compliant protocol and is beginning to approach HIV-positive kidney transplant candidates for enrollment.

"This program reflects the tremendous progress made in the last few decades in treating patients with HIV," says Christine Koval, MD, Section Head of Transplant Infectious Diseases in the

Department of Infectious Disease and principal investigator for Cleveland Clinic's HIV donor-positive to recipient-positive kidney transplant protocol. "Our ability to host this program at Cleveland Clinic is the result of collaboration between the Department of Infectious Disease and our robust kidney transplant team, led by Drs. Alvin Wee and Emilio Poggio. We are committed to providing access to transplantation for this patient population."

Reducing wait time, increasing therapeutic options

Patients with HIV have a higher risk of kidney disease and associated mortality and thus are likely to significantly benefit from the lifesaving therapy of kidney transplantation.

"We let patients know that being on the list for HIV-positive donor organs, in addition to remaining on the waitlist for HIV-negative donor organs, could reduce their wait times for kidney transplantation," says Dr. Modi. "We want HIV providers and nephrologists to know that their HIV-positive patients with end-stage kidney disease have this option, and we want HIV providers to tell their patients that they can be organ donors."

To refer a patient to the program, call 216.444.6996.

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Anita Modi, MD, is associate staff in the Department of Infectious Disease. She can be reached at modia@ccf.org or 216.636.1873. Christine Koval, MD, is Section Head of Transplant Infectious Diseases. She can be reached at kovalc@ccf.org or 216.636.1873.

INTRODUCING

Standardized Education in Ventilator Assistance (SEVA) VentRounds

SEVA VentRounds offers free, live, online training in using ventilator settings to evaluate the effectiveness of a patient's mechanical ventilation. Course instructors use standardized methods to read ventilator waveforms.

Held every other week on Tuesdays, 2-3 p.m. ET, each SEVA VentRounds session includes analysis of ventilator waveforms by course instructors and interactive discussion with participants.

This educational forum has been designed to benefit medical professionals who are (or have the equivalent medical education of) respiratory physicians, fellows or therapists.

Instructors:

- Eduardo Mireles-Cabodevila, MD
- Robert L. Chatburn, MHHS, RRT-NPS, FAARC

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clevelandclinic.org/VentRoundsWebX

Note: Registering on this page registers the participant for all sessions. View previously recorded sessions at **clevelandclinic.org/VentRounds**.

TREATING ALCOHOL USE DISORDER MAY HELP REDUCE DISEASE BURDEN IN ASTHMA AND COPD

KEY POINTS

A study is the first to link alcohol use disorder with increased hospitalizations and healthcare costs in patients with asthma or COPD.

A review of the records of more than 2 million patients with asthma or COPD found that those with alcohol use disorder were more likely to present with respiratory failure and require mechanical ventilation in the emergency department.

Pulmonologists can encourage patients to reduce alcohol use specifically to decrease the burden of respiratory disease.

More than 95,000 people in the U.S. die of alcohol-related causes each year, reports the Centers for Disease Control and Prevention. That number is likely underestimated, suggests Joe Zein, MD, PhD, MBA, a pulmonologist in Cleveland Clinic's Respiratory Institute.

"We know the direct impact of alcohol use disorder, but we don't know the indirect impact on other diseases," he says. "Excessive alcohol use can cause liver failure. It can blunt immune response and lead to malnutrition. But how does it affect outcomes in asthma, for example? The indirect burden of alcohol and substance use is equally important to our healthcare system and to society."

A study recently published in *Alcohol* explored the relationship.[1]

More respiratory failure, longer hospital stays

Dr. Zein and a research team analyzed the records of more than 2 million patients with asthma or chronic obstructive pulmonary disease (COPD) in the Nationwide Emergency Department Sample and 1.1 million in the 2012-2015 Nationwide Readmissions Database. They found that patients with alcohol use disorder were more likely to:

- Present with respiratory failure.
- Require mechanical ventilation in the emergency department (ED).
- Have a 5% longer length of stay when hospitalized.
- Have higher hospitalization costs.
- Be readmitted for asthma or COPD within 30 days.

"These findings really weren't surprising," says Dr. Zein. "The effects of alcohol, which can include higher risk of aspiration, infection and muscle wasting, can affect respiratory function and endurance, making respiratory failure more likely."

The study is the first to draw the distinct correlation between alcohol use disorder and adverse outcomes in asthma and COPD. It echoes the research team's 2020 study, published in the *Journal of Asthma*, which linked illegal drug use in the same cohort with higher healthcare use and cost.[2]

"The increase in disease morbidity persists even after adjusting for the effects of alcohol or substance misuse and related comorbidities," says Dr. Zein.

What it means for pulmonologists

This study may prompt more pulmonologists to ask about alcohol use and illicit drug use when managing patients with asthma or COPD, and potentially other respiratory diseases.

Alcohol use isn't an issue only for primary care, emphasizes Dr. Zein. If a primary care provider has already discussed reducing alcohol intake for the patient's overall health, a pulmonologist can

encourage reducing alcohol use specifically to decrease the burden of respiratory disease.

"We've been focused on reducing the cost and burden of asthma and COPD with better medication, better education and better follow-up," he says. "Now we have another method: treating alcohol use disorder."

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Joe Zein, MD, PhD, MBA, is staff in the Department of Pulmonary Medicine. He can be reached at zeinj@ccf.org or 216.445.1701.

REFERENCES

1. MacMurdo M, Lopez R, Udeh BL, Zein JG. Alcohol use disorder and healthcare utilization in patients with chronic asthma and obstructive lung disease. *Alcohol*. 2021;93:11-16.
2. MacMurdo M, Lopez R, Udeh BL, Zein J. Beyond tobacco — the secondary impact of substance misuse in chronic obstructive lung disease [published online ahead of print, 2020 Nov 19]. *J Asthma*. 2020;1-12.

SELECTED CLINICAL STUDIES

Consider offering your patients enrollment in a leading-edge clinical research trial at our Respiratory Institute. Contact the study coordinator or principal investigator for more information.

ALLERGY

Systemic Allergic Reactions to SARS-CoV-2 Vaccination

The study is designed with two principal aims: first, to estimate the proportions of systemic allergic reactions to the Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine in a high-allergy/mast cell disorder (HA/MCD) population; second, if the risk in HA/MCD is demonstrable, to determine whether the proportions are higher in the HA/MCD population compared to a non-atopic population.

Principal Investigator: David Lang, MD
Study Coordinator: JoAnne Baran-Smiley, BSN, RN | 216.444.5023

COPD

Roflumilast or Azithromycin to Prevent COPD Exacerbations (RELIANCE)

The objective of this study is to conduct a pragmatic, non-inferiority trial in a high-risk population of patients with COPD and chronic bronchitis to compare azithromycin to roflumilast for prevention of all-cause exacerbations.

Principal Investigator: Umur Hatipoglu, MD
Study Coordinator: Rick Rice, RRT | 216.444.1150

A Sham-Controlled Prospective Randomized Clinical Trial of the RejuvenAir® System for the Treatment of Moderate to Severe Chronic Obstructive Pulmonary Disease with Chronic Bronchitis (SPRAY-CB)

The primary objective of this trial is to demonstrate the safety and effectiveness of the RejuvenAir® System for the treatment of adult patients with a diagnosis of chronic bronchitis.

Principal Investigator: Thomas Gildea, MD
Study Coordinator: Yvonne Meli, RN, BC, CCRP | 216.445.4215

CRITICAL CARE MEDICINE

Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis (CLOVERS)

The objective of this NIH-sponsored trial is to determine the impact of a restrictive fluids strategy (vasopressors first, followed by rescue fluids) as compared to a liberal fluid strategy (fluids first, followed by rescue vasopressors) on 90-day in-hospital mortality in patients with sepsis-induced hypotension.

Principal Investigator: Abhijit Duggal, MD
Study Coordinator: Omar Mehkri | 216.445.1939

A Prospective, Multicenter, Randomized, Controlled, Pivotal Trial to Validate the Safety and Efficacy of the Hemolung® Respiratory Assist System for COPD Patients Experiencing an Acute Exacerbation Requiring Ventilatory Support (VENT-AVOID)

The primary objective of this study is to demonstrate the safety and efficacy of using the Hemolung® Respiratory Assist System to provide low-flow ECCO2R as an alternative or adjunct to invasive mechanical ventilation versus standard-of-care invasive mechanical ventilation alone to increase ventilator-free days for COPD patients who require respiratory support due to an acute exacerbation of their COPD.

Principal Investigator: Abhijit Duggal, MD
Study Coordinator: Omar Mehkri | 216.445.1939

A Protocol Comparing Temporary Transvenous Diaphragm Pacing to Standard of Care for Weaning from Mechanical Ventilation in ICU Patients (RESCUE 3)

The goal of this study is to investigate the safe and effective performance of the Lungpacer Diaphragm Pacing Therapy System in patients who have failed to wean from mechanical ventilation.

Principal Investigator: Tarik Hanane, MD
Study Coordinator: Bryan Poynter | 216.445.1630

Bacteremia Antibiotic Length Actually Needed for Clinical Effectiveness: a Randomized Controlled Trial (BALANCE)

This is a non-inferiority, concealed allocation trial of shorter duration (7 days) versus longer duration (14 days) antibiotic treatment for critically ill patients with bloodstream infections.

Principal Investigator: Abhijit Duggal, MD
Study Coordinator: Bryan Poynter | 216.445.1630

Cooling to Help Injured Lungs (CHILL) Phase IIb Randomized Controlled Trial of Therapeutic Hypothermia in Patients with ARDS

The objective of this DOD-sponsored trial is to test the hypothesis that early treatment with mild induced hypothermia along with neuromuscular blockade to prevent shivering will be beneficial for patients with acute respiratory distress syndrome (ARDS).

Principal Investigators: Abhijit Duggal, MD; Rachel Scheraga, MD
Study Coordinator: Omar Mehkri | 216.445.1939

Evaluation of Vaccine-Induced Anti-SARS-CoV-2 Activity Against Emerging SARS-CoV-2 Variant

The objective of this study is to test individuals vaccinated with SARS-CoV-2 vaccines who have no known history of a previous SARS-CoV-2 infection to assess vaccine-induced activity against emerging SARS-CoV-2 variants.

Principal Investigator: Abhijit Duggal, MD
Study Coordinator: Meg Mitchell | 216.445.1939

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CYSTIC FIBROSIS

Cystic Fibrosis Foundation Patient Registry

The Cystic Fibrosis (CF) Patient Registry collects information on the health status of people with cystic fibrosis who receive care in CF Foundation-accredited care centers and agree to participate in the registry. This information is used to create CF care guidelines, assist care teams providing care to individuals with CF, and guide quality improvement initiatives at care centers. Researchers also use the patient registry to study CF treatments and outcomes and to design CF clinical trials.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: David Weaver, BSN, CCRC | 216.445.6671

Cystic Fibrosis Lung Transplant Consortium

The objective of this proposal is the establishment of a clinical and translational research network of CF lung transplant centers to facilitate the study of lung transplant for CF and other lung diseases to improve access, clinical care and long-term outcomes of individuals with CF who undergo lung transplant.

Principal Investigator: Maryam Valapour, MD
Study Coordinator: David Weaver, BSN, CCRC | 216.445.6671

A Protocol to Test the Impact of Discontinuing Chronic Therapies in People with Cystic Fibrosis on Highly Effective CFTR Modulator Therapy (SIMPLIFY)

The goal of this study is to determine whether discontinuing hypertonic saline or dornase alfa is non-inferior to continuing after establishment of chronic ETI.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: David Weaver, BSN, CCRC | 216.445.6671

A Phase 4 Study to Compare U.S.-Marketed Creon® Drug Product with Drug Product Manufactured with a Modernized Process at an Alternate Manufacturing Site, in Subjects with EPI due to Cystic Fibrosis

The objective of the study is to compare pancrelipase delayed-release (DR) capsules modernized process drug product to an active control (pancrelipase DR capsules currently marketed in the U.S. as Creon®) in subjects with exocrine pancreatic insufficiency (EPI) due to cystic fibrosis.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: David Weaver, BSN, CCRC | 216.445.6671

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INFECTIOUS DISEASE

Prospective Observational Study of Human Immunodeficiency Virus (HIV)-Positive Deceased Donor Renal Transplantation for HIV-Positive Recipients

This research is being done to learn whether organ transplantation from HIV-positive deceased donors is as safe and effective in HIV-positive recipients as transplants from HIV-negative deceased donors.

Principal Investigator: Christine Koval, MD
Study Coordinator: Kiran Ashok | 216.445.6744

A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of NPC-21 for Kidney Transplant Recipients at High Risk of Cytomegalovirus Infection (LIONHEART21)

This is a phase 2, randomized, double-blind, placebo-controlled study of NPC-21 for kidney transplant recipients at high risk of cytomegalovirus infection in the United States and Japan.

Approximately 108 eligible patients will be randomized prior to first study drug administration to receive low-dose NPC-21, high-dose NPC-21 or placebo.

Principal Investigators: Aneela Majeed, MD; Christine Koval, MD
Study Coordinator: Kiran Ashok | 216.538.9139

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INTERSTITIAL LUNG DISEASE

Chronic Fibrosing Interstitial Lung Disease with Progressive Phenotype Prospective Outcomes (ILD-PRO) Registry

This registry is a prospective registry that will collect information regarding treatment of participants with a diagnosis of a chronic fibrosing interstitial lung disease with progressive phenotype.

Principal Investigator: Daniel Culver, DO
Study Coordinator: Sue Gole, RRT | 216.445.5836

A Phase I, Double-Blind, Placebo-Controlled, Single and Multiple Inhaled Dose, Safety, Tolerability and Pharmacokinetic Study of TRK-250 in Subjects with Idiopathic Pulmonary Fibrosis

The principal aim of this study is to obtain safety and tolerability data when TRK-250 is administered by inhalation as single and multiple doses to subjects with idiopathic pulmonary fibrosis.

Principal Investigator: Daniel Culver, DO
Study Coordinator: Ron Wehrmann, RRT | 216.445.0574

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LUNG CANCER

DECAMP 1 PLUS Proposal: Prediction of Lung Cancer Using Noninvasive Biomarkers

The objective of this study is to determine if individual or combinations of clinical, molecular and imaging features can reliably identify individuals with indeterminate lung nodules 8-25 mm who have lung cancer.

Principal Investigator: Peter Mazzone, MD
Study Coordinator: Stuart Houltham | 216.444.1056

DNA Evaluation of Fragments for Early Interception — Lung Cancer Training Study (DELFI-L101 Study)

The primary objective of this study is to train and test classifiers for lung cancer detection using the DELFI assay and other biomarkers and clinical features.

Principal Investigator: Peter Mazzone, MD
Study Coordinator: Stuart Houltham | 216.445.1056

Nodify XL2 Classifier Clinical Utility Study in Low- to Moderate-Risk Lung Nodules (ALTITUDE)

This study evaluates how addition of the Nodify XL2 test result impacts the clinical management of new, incidentally identified solid lung nodules assessed as low to moderate risk of cancer.

Principal Investigator: Peter Mazzone, MD
Study Coordinator: Stuart Houltham | 216.445.1056

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LUNG TRANSPLANT

Improving Frailty with a Rigorous Ambulation Intervention in Lung Transplant Patients (iFRAIL)

The objective of this study is to evaluate frailty pre- and post-transplant to determine the effect of dedicated ambulator-assisted physical activity in lung transplant inpatients.

Principal Investigator: Marie Budev, DO, MPH
Study Coordinator: Abigail Camiener | 216.444.8347

A Phase III, Prospective, Multicenter, Randomized, Controlled Clinical Trial to Demonstrate the Effectiveness and Safety of Liposomal Cyclosporine A (L-CsA) Inhalation Solution Delivered via the PARI Investigational eFlow® Device Plus Standard of Care Versus Standard of Care Alone in the Treatment of Bronchiolitis Obliterans Syndrome in Patients Post Lung Transplantation (BOSTON-1 and BOSTON-2)

The objective of the trial is to assess the efficacy and safety of add-on aerosolized L-CsA to standard-of-care therapy as compared to standard-of-care therapy alone in the treatment of bronchiolitis obliterans syndrome in lung transplant recipients.

Principal Investigator: Marie Budev, DO, MPH
Study Coordinator: Valerie Shaner, RRT | 216.444.3766

An Open-Label, Single-Arm, Phase 1/2 Study Evaluating the Safety and Efficacy of Itacitinib in Participants with Bronchiolitis Obliterans Syndrome Following Lung Transplantation

The purpose of this study is to test itacitinib, a JAK inhibitor, to identify an appropriate dose as a treatment for patients with bronchiolitis obliterans syndrome following lung transplantation.

Principal Investigator: Marie Budev, DO, MPH
Study Coordinator: JoAnne Baran-Smiley, BSN, RN | 216.444.5023

Cleveland Clinic Lung Transplant Biorepository

The aim of this program is to establish a patient-linked biological sample repository for use in future research studies related to metabolic, inflammatory and immunologic markers related to organ transplantation in general and lung transplantation in particular.

Principal Investigator: Maryam Valapour, MD
Study Coordinator: David Weaver, BSN, CCRC | 216.445.6671

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PULMONARY HYPERTENSION

Pulmonary Hypertension Research Registry

The Pulmonary Hypertension Research Registry is a collection of patients' clinical and demographic data to be used for future research. The purpose of this registry is to develop a list of prospective participants with pulmonary hypertension who are interested in learning about future research opportunities. In addition to being part of the registry, participants will receive quarterly newsletters including information about recent research findings in pulmonary hypertension, currently enrolling and upcoming studies, and more.

Principal Investigator: Kristin Highland, MD
Study Coordinator: Mary Beukemann | 216.444.2140

Study Evaluating the Efficacy and Safety of Ralinepag to Improve Treatment Outcomes in PAH Patients (ADVANCE Outcomes)

The primary objective of this Arena-sponsored study is to compare the effect of ralinepag versus placebo in subjects with standard of care or PAH-specific background therapy on disease progression and achievement of a satisfactory clinical response in subjects with WHO Group 1 PAH.

Principal Investigator: Alice Goyanes, MD
Study Coordinator: Mary Beukemann | 216.444.2140

Pulmonary Arterial Hypertension Improvement with Nutrition and Exercise (PHINE) — a Randomized Controlled Trial

The National Institutes of Health is funding this study to assess the effect of diet and exercise on metabolism and its role in pulmonary hypertension. This is a 12-week diet and exercise study that has five days a week of exercise training and one day a week of diet counseling.

Principal Investigator: Gustavo Heresi, MD
Study Coordinators: Chazity Bush | 216.444.3702; Celia Melillo | 216.445.3763

A Phase 3, Randomized, Placebo-Controlled, Double-Blind, Adaptive Study to Evaluate the Safety and Efficacy of Inhaled Treprostinil in Patients with Pulmonary Hypertension Due to Chronic Obstructive Pulmonary Disease (PH-COPD) — (PERFECT)

The objective of this study is to demonstrate the efficacy of inhaled treprostinil in improving exercise ability as measured by change from baseline in 6-minute walk distance (6MWD) in subjects with PH-COPD.

Principal Investigator: Joseph Parambil, MD
Study Coordinator: Mary Beukemann | 216.444.2140

Selexipag in Inoperable or Persistent/Recurrent Chronic Thromboembolic Pulmonary Hypertension (SELECT)

This phase 3 study will assess the efficacy and safety of selexipag as an add-on to standard-of-care therapy in subjects with inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension after surgical and/or interventional treatment.

Principal Investigator: Gustavo Heresi, MD
Study Coordinator: Julia Ashton | 216.445.7075

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RARE LUNG DISEASES

ALPHA-1 ANTITRYPSIN DEFICIENCY

Alvelestat (MPH996) for the Treatment of Alpha-1 Antitrypsin Deficiency (ATALANTa)

This NCATS-sponsored, phase 2, multicenter, double-blind, randomized (1:1), placebo-controlled proof-of-concept study is designed to evaluate the safety and tolerability as well as the mechanistic effect of oral administration of alvelestat (MPH996) in subjects with confirmed alpha-1 antitrypsin deficiency-related emphysema.

Principal Investigators: Umur Hatipoglu, MD; James Stoller, MD
Study Coordinator: Rick Rice, RRT | 216.444.1150

BRONCHIECTASIS

Clinical Effectiveness of High-Frequency Chest Wall Oscillation (HFCWO) in a Bronchiectasis Population

The primary objective is to evaluate the impact of HFCWO use on patients' quality of life.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: Valerie Shaner, RRT | 216.444.3766

ARISE — a Randomized, Double-Blind, Placebo-Controlled, Active-Comparator Multicenter Study to Validate Patient-Reported Outcome Instruments in Adult Subjects with Newly Diagnosed Nontuberculous Mycobacterial (NTM) Lung Infection Caused by *Mycobacterium avium* Complex (MAC)

The goal of this study is to validate the patient-reported outcome measures in this patient population.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: Valerie Shaner, RRT | 216.444.3766

ENCORE — a Randomized, Double-Blind, Placebo-Controlled, Active-Comparator Multicenter Study to Evaluate the Efficacy and Safety of an Amikacin Liposome Inhalation Suspension (ALIS)-Based Regimen in Adult Subjects with Newly Diagnosed Nontuberculous Mycobacterial (NTM) Lung Infection Caused by *Mycobacterium avium* Complex (MAC)

The objective of this study is to evaluate the efficacy of ALIS in adults with newly diagnosed (initial or subsequent) MAC lung infections.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: Valerie Shaner, RRT | 216.444.3766

ASPEN — a Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Multicenter Study to Assess the Efficacy, Safety and Tolerability of INS1007 Administered Once Daily for 52 Weeks in Subjects with Non-Cystic Fibrosis Bronchiectasis

The primary objective of this study is to evaluate the effect of brensocatib at 10 mg and 25 mg compared with placebo on the rate of pulmonary exacerbations over the 52-week treatment period.

Principal Investigator: Elliot Dasenbrook, MD
Study Coordinator: Valerie Shaner, RRT | 216.444.3766

PULMONARY ALVEOLAR PROTEINOSIS

A Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Once-Daily Inhaled Molgramostim Nebulizer Solution in Adult Subjects with Autoimmune Pulmonary Alveolar Proteinosis (aPAP)

The goal of this study is to investigate the efficacy of molgramostim, an inhaled form of the recombinant human granulocyte macrophage colony stimulating factor (rhGM-CSF) in subjects with aPAP.

Principal Investigator: Daniel Culver, DO
Study Coordinator: Sue Gole, RRT | 216.445.5836

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SARCOIDOSIS

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study in Participants with Sarcoidosis-Associated Pulmonary Hypertension (SAPH) to Assess the Efficacy and Safety of Oral Selexipag

The goal of this trial is to assess the effect of selexipag versus placebo on pulmonary vascular resistance in participants with sarcoidosis-associated pulmonary hypertension.

Principal Investigator: Joseph Parambil, MD
Study Coordinators: Mary Beukemann | 216.444.2140; Allison Wimer, RRT | 216.445.9557

Acthar® Gel for Cutaneous Sarcoidosis

Supported by Mallinckrodt ARD and Albany Medical College, this study aims to provide evidence that Acthar® gel may serve as a therapeutic immune-modulating alternative to glucocorticoids in patients with active cutaneous sarcoidosis.

Principal Investigator: Manuel Ribeiro, MD
Study Coordinator: JoAnne Baran-Smiley, BSN, RN | 216.444.5023

Routine Cardiac Screening in Sarcoidosis Patients (PAPLAND)

This is an unblinded, randomized screening trial for cardiac sarcoidosis in patients seen during routine clinical care who have not been clinically suspected to have cardiac sarcoidosis according to conventional criteria, comparing the addition of echocardiogram and ambulatory ECG to usual clinical follow-up.

Principal Investigator: Daniel Culver, DO
Study Coordinator: Allison Wimer, RRT | 216.445.9557

Prospective Registry of Outcomes in Myocardial Sarcoidosis (PROMyS)

This is a prospective multicenter registry of incident cases of confirmed or suspected cardiac sarcoidosis.

Principal Investigator: Manuel Ribeiro, MD
Study Coordinator: Allison Wimer, RRT | 216.445.9557

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ABOUT CLEVELAND CLINIC

Cleveland Clinic is a nonprofit, multispecialty academic medical center integrating outpatient and hospital care with research and education for better patient outcomes and experience. More than 4,500 staff physicians and researchers provide services through 20 patient-centered institutes. Cleveland Clinic is a 6,026-bed healthcare system with a main campus in Cleveland, 18 hospitals and over 220 outpatient locations. The health system includes five hospitals in Southeast Florida with more than 1,000 beds, a medical center for brain health in Las Vegas, a sports and executive health center in Toronto, and a 364-bed hospital in Abu Dhabi. Cleveland Clinic London, a 184-bed hospital, will open in 2022. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*.

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