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[1]Hasani A et al. *Chron Respir Dis*. 2008;5(2):81-86. [2] Roca O et al. *Respir Care*. 2010;55(4):408-413.

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News

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SpiroHome Erratum

In the Fall 2019 issue of RT magazine, we published an article on "Understanding Why Not All FDA Cleared Spirometers Should Be Used for COPD Patients". This article explored how the 2005 ATS/ERS testing specifications did not actually test whether spirometers could accurately measure low flow as well as presenting test data on spirometers used for home measurements.

One of the spirometers we tested and reported failing to meet the low flow ATS/ERS requirement was the Inofab Health, SpiroHome. Following a discussion with the manufacturer, we found that the spirometer failed to accurately measure low flow when we did not perform a sensor "zero" before each measurement, which was not enforced. The manufacturer has subsequently modified their application software and we therefore went back and tested the spirometer using their new software. Using their new application, the SpiroHome accurately measured volumes to within 2% of the actual volume, even at flows at the ATS/ERS minimum flow requirement of 0.025 L/sec. We are pleased that they have made the appropriate changes.

Stenzler A, Stegenga M. Understanding Why Not All FDA Cleared Spirometers Should Be Used for COPD Patients. Respiratory Therapy 2019; 14(4):18-20

SARS-CoV-2 Testing Portfolio Detects Omicron Variant

Siemens Healthineers has announced that the company's SARS-CoV-2 tests are well designed to detect the Omicron SARS-CoV-2 variant. The company recently evaluated the potential impact of the emergent variant on the CLINITEST Rapid COVID-19 Antigen Test, the FTD SARS-CoV-2 Assay, a PCR test, and the Atellica IM / ADVIA Centaur SARS-CoV-2 Antigen Assay (CoV2Ag). On November 26, 2021, both the WHO and ECDC designated the Omicron variant as a variant of concern. Mutations are normal, abundant, and expected, especially with an RNA virus, and the SARS-CoV-2 is no different. As countries struggle to combat emerging variants, fast and accurate testing is an important tool in containing spread.
To assess the potential impact to the CLINITEST rapid test and the Atellica/ADVIA Centaur SARS-CoV-2 Antigen (CoV2Ag) Assay, the Siemens Healthineers R&D team analyzed the sequence data of the Omicron variant nucleocapsid protein. This analysis demonstrated >98% sequence homology of the nucleocapsid protein to other SARS-CoV-2 variants. Meaning, it is unlikely that the Omicron variant would affect the results. The CLINITEST Rapid COVID-19 Antigen Self-Test has a sensitivity of 97.25 percent and a specificity of 100 percent (compared to a PCR, or nucleic acid-detection method) and provides results in 15 minutes. The simple process for collecting a nasal swab and obtaining a result are included in the Instructions for Use. A nasal swab is collected from both nostrils and then the swab is washed in a buffer to reveal a specific protein inside the SARS-CoV-2 virus. The sample is then dispensed onto the test cassette and after 15 minutes the result is visible. The position and number of lines clearly indicate whether the test is positive or negative. The Siemens Healthineers' CoV2Ag test shows strong alignment compared with on the market available automated real-time (RT)-PCR testing with sensitivity exceeding 96% and specificity exceeding 99% for the Atellica CoV2Ag test. While molecular RT-PCR diagnostic testing is the gold standard in accuracy, it lacks the high throughput capability of a lab-based, automated antigen test. With availability of CoV2Ag on the Atellica IM Analyzer, laboratories can significantly increase the SARS-CoV-2 testing capacity with a platform that can run up to 440 tests per hour. Siemens Healthineers has also confirmed, based on in silico analysis, that the FTD SARS-CoV-2 Assay, a PCR-based test, detects the Omicron variant. Dual target design makes it possible to detect two different genomic regions of SARS-CoV-2. One benefit of this is a higher sensitivity because it is possible to detect two

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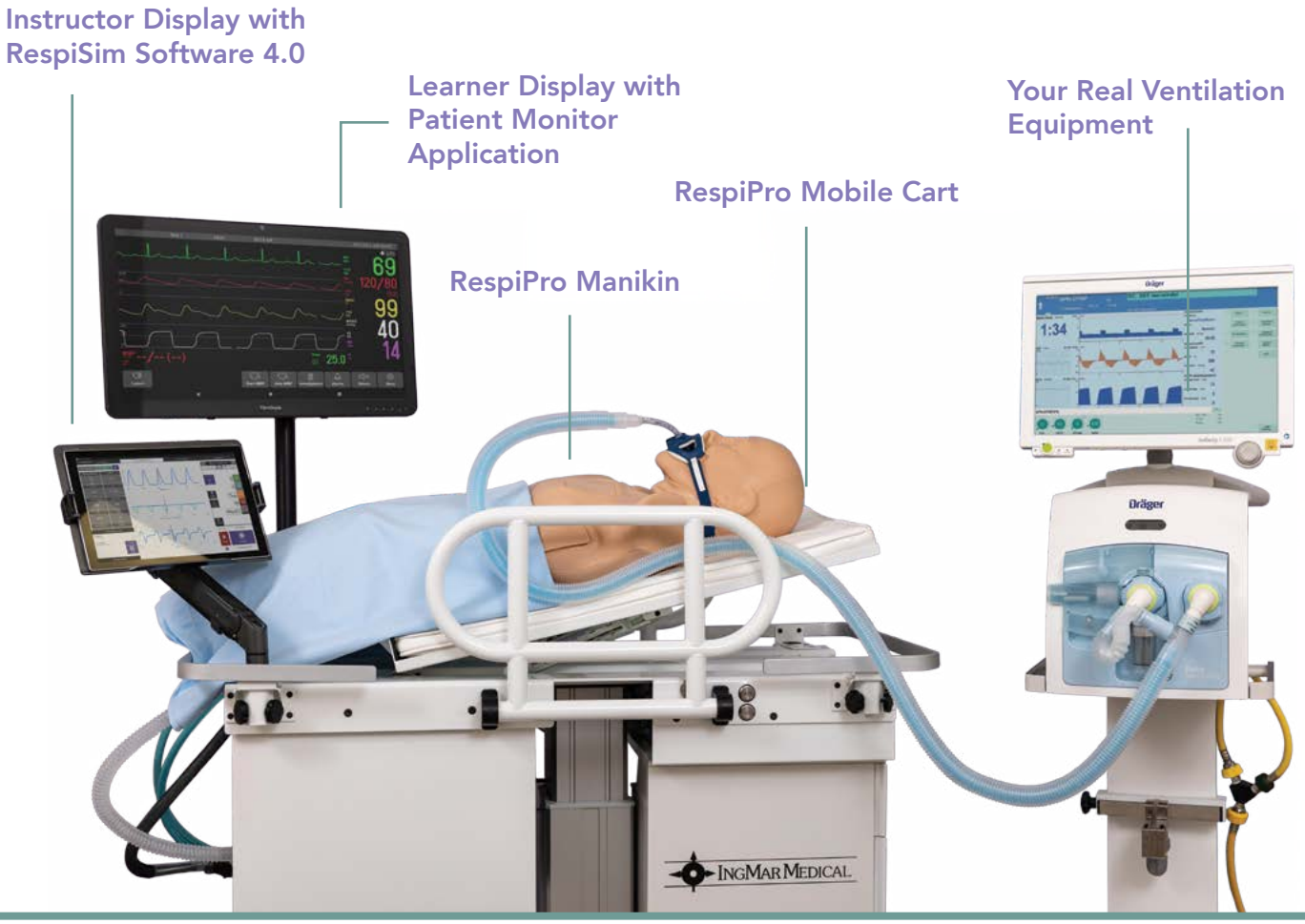

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different genomic regions on the same detection channel, but most important right now, is that it helps to cope with mutations. Siemens Healthineers offers an evolving menu of single mutation PCR reflex tests that complement our FTD SARS-CoV-2 Assay to identify SARS-CoV-2 variants. Our relationship with A1 Life Sciences allows us to offer research use only tests (RUO). that enable laboratories to efficiently detect mutations to discriminate between circulating variants, including Omicron. "As a leader in laboratory diagnostics, Siemens Healthineers is committed to monitoring all current and emerging variants of concern to ensure the test results remain accurate and reliable," said Deepak Nath, PhD, President Laboratory Diagnostics, Siemens Healthineers. "Accurate diagnostic tools are a critical factor in allowing public health authorities to combat the spread of virus and protect the health of their populations."

What We Know, What We Don't About the Omicron Variant

A new COVID-19 variant known as Omicron has global health officials concerned as scientists race to discover how mutations will impact the transmission and severity of the virus. Here's what we know. Omicron, officially known as B.1.1.529, was designated a variant of concern on November 26 by the World Health Organization (WHO). The designation was made based on evidence presented to the WHO's Technical Advisory Group on Virus Evolution that Omicron has several mutations that may affect how the variant behaves, ie, the severity of disease it causes, its degree of transmissibility, and the variant's immune escape potential—that is, whether it can bypass protection offered by current COVID-19 vaccines. Omicron was first identified in South Africa and reported to the WHO on November 24; it has now been detected in Australia, Belgium, Botswana, Britain, Denmark, Germany, Hong Kong, Israel, Italy, the Netherlands, France, Canada, and South Africa. At least 44 countries have imposed travel restrictions from several African countries, reports CNN. Japan and Israel have banned all foreign nationals from entering their countries. Health officials in Canada confirmed the country's first 2 cases in Ottawa, November 28. There have been 50 mutations identified in the B.1.1.529 lineage, the most concerning being more than 30 in the spike protein region, the area that facilitates a virus' entry into the host cell, enhancing its transmissibility as well as the potential for immunoescape. WHO notes, however, that it is not clear yet whether the variant is more transmissible compared to other recent variants, including Delta. While the number of persons testing positive for Omicron has increased in areas of South Africa where circulation has been identified, studies have been launched to understand if the variant is to blame or if other factors may be implicated. There are as yet no data to clarify whether Omicron causes more severe disease compared to other variants, and WHO again points to Delta as the primary comparator. "Preliminary data suggest that there are increasing rates of hospitalization in South Africa, but this may be due to increasing overall numbers of people becoming infected, rather than a result of specific infection with Omicron," states WHO. Nor is there any suggestion that symptoms associated with Omicron infection are different from those seen with currently circulating variants. According to a report from Reuters, a South African physician who was among the first clinicians to suspect a different strain of the coronavirus among patients he saw said that "the symptoms of the Omicron variant were so far mild and could be treated at home." The chair of South African Medical Association, also speaking, said that no patients so far have reported loss of smell or taste and there has been no major drop in oxygen levels observed. According to WHO, initial reported infections were among university students who overall tend to have milder infection and symptoms. Better understanding of both infectivity and transmissibility of Omicron will likely take several weeks, the WHO stressed, as will accruing information on whether the variant can potentially render current vaccinations less effective. "Work is already under way to look at the immune escape potential of B.1.1.529 in the laboratory setting," note scientists with South Africa's National Institute for Communicable Diseases (NICD) in a statement. "Based on our understanding of the mutations in this lineage, partial immune escape is likely, but it is likely that vaccines will still offer high levels of protection against hospitalization and death." Effectiveness of current tests is currently not in question, according to WHO, as the widely used PCR assays continue to detect infection, including with Omicron. Research is underway to assess any potential impact of the variant on other tests including rapid antigen detection tests. Treatments for COVID-19 also are being assessed for efficacy against Omicron infection but WHO stresses that both corticosteroids and IL-1 receptor antagonists will continue to be effective against severe COVID-19. In statements, leaders from both Pfizer-BioNTech and Moderna said virus mutations have been anticipated since the beginning and that the companies are working closely with authorities to process information as soon as it is available.

Merck's COVID-19 Pill May Be Less Effective Than First Hoped

Merck's antiviral pill for COVID-19, molnupiravir, appears to be far less effective than early results from the clinical trial first suggested. According to an analysis by scientists at the FDA, the experimental pill cut the risk of hospitalization or death from COVID-19 by about 30%, compared to a placebo, and the pill showed no benefit for people with antibodies against COVID-19 from prior infection. The updated analysis showed 48 hospitalizations or deaths among study participants who were randomly assigned to take the antiviral drug, compared to 68 among those who took a placebo. Those results come from the full set of 1,433 patients who were randomized in the clinical trial, which just became available last week. Initial results from the first 775 patients enrolled in the clinical trial, which were issued in a company news release in October, had said the drug cut the risk of hospitalization or death for patients at high risk of severe disease by about 50%. Merck has been producing millions of doses of molnupiravir, which is the first antiviral pill to treat COVID-19 infections. The United Kingdom's drug regulator authorized use of the medication in early November. The company said it expected to distribute the medication globally by the end of 2021. Last month, two Indian drug companies halted late-stage clinical trials of a generic version of molnupiravir after the studies failed to find any benefit to patients with moderate COVID-19. Trials in patients with milder symptoms are still ongoing. *TheNew England Journal of Medicine* postponed its planned early release of the molnupiravir study results, citing "new information." The medication is designed to be given as four pills taken every 12 hours for 5 days. It's most effective when taken within the first few days of new symptoms, something that requires convenient and affordable testing. The new results seem to put molnupiravir far below the effectiveness of existing treatments.

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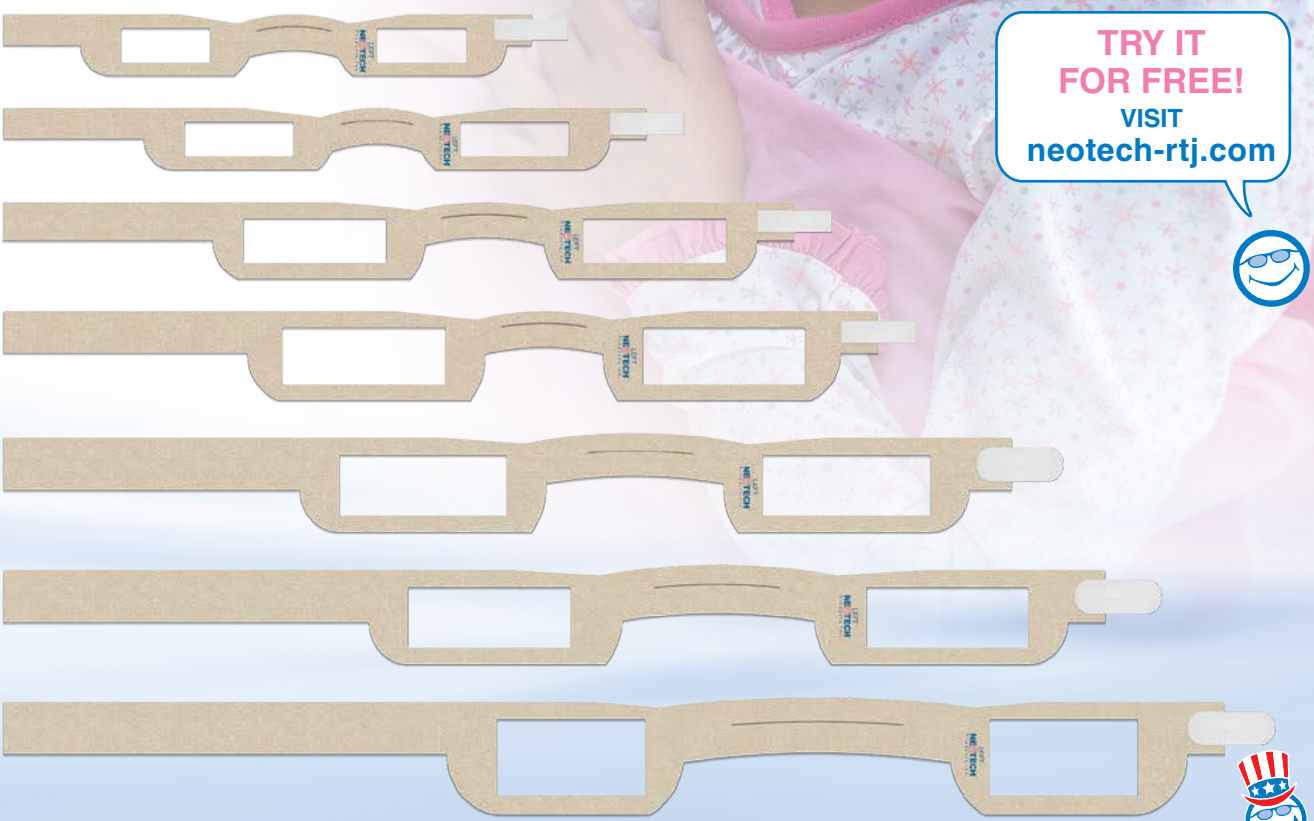

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Rhinosinusitis Without Nasal Polyps Lowers QoL in COPD

Concomitant rhinosinusitis without nasal polyps (RSsNP) in patients with chronic obstructive pulmonary disease (COPD) is associated with a poorer, disease-specific, health-related quality of life (HRQoL), a Norwegian study is showing. "Chronic rhinosinusitis has an impact on patients' HRQoL," lead author Marte Rystad Øie, Trondheim University Hospital, Trondheim, Norway, said in an email. "We found that RSsNP in COPD was associated with more psychological issues, higher COPD symptom burden, and overall COPD-related HRQoL after adjusting for lung function, so RSsNP does have clinical relevance and [our findings] support previous studies that have suggested that rhinosinusitis should be recognized as a comorbidity in COPD," she emphasized. The study sample consisted of 90 patients with COPD and 93 control subjects, all age 40-80 years. "Generic HRQoL was measured with the Norwegian version of the SF-36v2 Health Survey Standard questionnaire," the authors write, and responses were compared between patients with COPD and controls as well as between subgroups of patients who had COPD both with and without RSsNP. Disease-specific HRQoL was assessed by the Sinonasal Outcome Test-22 (SNOT-22); the St. Georges Respiratory Questionnaire (SGRQ), and the COPD Assessment Test (CAT), and responses were again compared between patients who had COPD with and without RSsNP. In the COPD group, "severe" and "very severe" airflow obstruction was present in 56.5% of patients with RSsNP compared with 38.6% of patients without RSsNP, as Øie reports. Furthermore, total SNOT-22 along with psychological subscale scores were both significantly higher in patients who had COPD with RSsNP than those without RSsNP. Among those with RSsNP, the mean value of the total SNOT-22 score was 36.8 whereas the mean value of the psychological subscale score was 22.6. Comparable mean values among patients who had COPD without RSsNP were 9.5 and 6.5, respectively ($P < .05$). Total scores on the SGRQ were again significantly greater in patients who had COPD with RSsNP at a mean of 43.3 compared with a mean of 34 in those without RSsNP, investigators observe. Similarly, scores for the symptom and activity domains again on the SGRQ were significantly greater for patients who had COPD with RSsNP than those without nasal polyps. As for the total CAT score, once again it was significantly higher in patients who had COPD with RSsNP at a mean of 18.8 compared with a mean of 13.5 in those without RSsNP ($P < .05$). Indeed, patients with RSsNP were four times more likely to have CAT scores indicating the condition was having a high or very high impact on their HRQoL compared with patients without RSsNP ($P < .001$). As the authors point out, having a high impact on HRQoL translates into patients having to stop their desired activities and having no good days in the week. "This suggests that having RSsNP substantially adds to the activity limitation experienced by patients with COPD," they emphasize. The authors also found that RSsNP was significantly associated with poorer physical functioning after adjusting for COPD as reflected by SF-36v2 findings, again suggesting that patients who had COPD with concomitant RSsNP have an additional limitation in activity and a heavier symptom burden. As Øie explained, rhinosinusitis has two clinical phenotypes: that with nasal polyps and that without nasal polyps, the latter being twice as prevalent. In fact, rhinosinusitis with nasal polyps is associated with asthma, as she pointed out. Given, however, that rhinosinusitis without polyps is amenable to treatment with daily use of nasal steroids, it is possible to reduce the burden of symptoms and psychological stress associated with RSsNP in COPD. Limitations of the study include the fact that investigators did not assess patients for the presence of any comorbidities that potentially could contribute to poorer HRQoL in this patient population.

Sleep-Disordered Breathing Could Inflate Risk for Severe COVID-19

People with sleep-disordered breathing or sleep-related hypoxia—low oxygen levels during sleeping—are no more likely than other adults to get infected with SARS-CoV-2 and develop COVID-19. However, if infected, they are at a 31% higher risk of getting hospitalized or dying from the illness, new research reveals. Investigators looked at almost 360,000 patients tested for COVID-19 at the Cleveland Clinic system. This group included 5400 people who also completed a sleep study. They also accounted for other factors that could alter COVID-19 risk, including obesity, heart and lung disease, cancer, and smoking. "In those with COVID-19, baseline oxygen lowering during sleep was associated with increased association with hospitalization and mortality, even after consideration of factors which could confound this relationship," Cinthya Pena Orbea, MD, said. When asked if she was surprised by the 31% increased risk, Pena Orbea said, "While this was consistent with our a priori hypotheses and we were careful to take in to account pulmonary disease and smoking history, we still identified a statistically significant association." Pena Orbea is on staff at the Sleep Disorder Center and is assistant professor of medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University in Ohio. Identifying another group at potentially higher risk for adverse outcomes could help allocate COVID-19 resources

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earlier or more appropriately, senior study author Reena Mehra, MD, director of sleep disorder research at Cleveland Clinic, said in a news release. "As the COVID-19 pandemic continues and the disease remains highly variable from patient to patient, it is critical to improve our ability to predict who will have more severe illness," she said.

Novel Bronchoscopic Interventions Appear Promising for Patients With COPD

Several emerging bronchoscopic treatments have the potential to improve the quality of life for patients with chronic obstructive pulmonary disease, an investigator reported at the annual meeting of the American College of Chest Physicians. Targeted lung denervation is one promising novel therapeutic option that is safe and may improve clinical outcomes according to investigator Christian Ghattas, MD. Data from an ongoing phase 3 randomized controlled trial may provide new information on the efficacy of targeted lung denervation in patients with chronic obstructive pulmonary disease (COPD), said Dr Ghattas, assistant professor of medicine and associate program director for the interventional pulmonary fellowship at The Ohio State University Medical Center in Columbus. "Outcome data of longer follow-up on previously treated patients will provide us with more information on the durability and the effect of this treatment," Ghattas said in an online presentation at the CHEST meeting, which was held virtually this year. Meanwhile, a few compelling bronchoscopic treatment modalities for patients with chronic bronchitis are in earlier stages of clinical development. "Larger randomized, controlled trials are ongoing to confirm the available data and to evaluate treatment durability," said Dr. Ghattas. The targeted lung denervation system under study (dNerva®, Nuvaira Inc.) involves the use of a radiofrequency catheter to ablate the peribronchial branches of the vagus nerve, Dr Ghattas said. The goal of disrupting pulmonary nerve input is to achieve sustained bronchodilation and reduce mucous secretion, thereby simulating the effect of anticholinergic drugs, he added. In pilot studies, the targeted lung denervation system demonstrated its feasibility and safety, while modifications to the system reduced the rate of serious adverse events, according to Dr Ghattas. In the AIRFLOW-1 study, which evaluated the safety of the latest generation version of the system, 30 patients with COPD were randomized to targeted lung denervation at one of two doses, 29 or 32 watts. Of those 30 patients, 29 (96.7%) had procedural success, meaning the catheter was inserted, guided to its intended location, and removed intact with no reported in-hospital serious adverse events, according to results published in Respiration. There was no difference between arms in the primary endpoint, which was the rate of adverse airway effects requiring intervention that were associated with targeted lung denervation, investigators reported. Four such events occurred, in 3 of 15 patients treated with 32 watts and 1 of 15 patients treated with 29 watts. Procedural success, defined as device success without an in-hospital serious adverse event, was 96.7% (29/30). The rate of TLD-associated adverse airway effects requiring intervention was 3/15 in the 32 W versus 1/15 in the 29 W group (P = .6). However, serious gastric events were noted in five patients, prompting safety improvements and procedural enhancements that reduced both gastrointestinal and airway events, according to the study report.

COVID-19 Pandemic Fueled the Growth of Telemedicine in Allergy

The use of telemedicine has historically been low among allergy practitioners compared with other specialists, but the pandemic has accelerated the growth of virtual allergy visits. "My own practice went from zero to 100% telemedicine in a matter of days," Susan Bailey, MD, an allergist at Fort Worth Allergy and Asthma Associates, in Fort Worth, Texas, and immediate past president of the American Medical Association, said during a plenary session at the American College of Allergy, Asthma, and Immunology (ACAAI) 2021 Annual Meeting, held in New Orleans. "I think the pandemic really pushed people out of necessity to adopt telehealth, or really decide if it's for them or not, quicker than they might have," said Melinda Rathkopf, MD, director of the Allergy, Asthma and Immunology Center of Alaska, in Anchorage, in an interview before co-moderating a telemedicine session at the conference. Across medicine, practitioners are seeing 50 to 175 times the number of patients through telehealth than they were before the COVID-19 pandemic, and nearly half of doctors are continuing to use telehealth as the pandemic causes shifts in practice patterns and the delivery of care. These trends are shown in McKinsey survey data that were presented at the ACAAI meeting by Jennifer Shih, MD, allergist-immunologist and assistant professor of pediatrics and internal medicine at Emory University, in Atlanta, Georgia. Several factors allowed telemedicine to grow. During the pandemic, the US Department of Health and Human Services relaxed the requirement that telehealth delivery be HIPAA compliant. Thus, physicians were able to use Zoom, Skype, Facetime, and other everyday technologies for virtual visits. In addition, the Centers for Medicare & Medicaid Services (CMS) instituted a number of changes to make telehealth more accessible — among them, recognizing a patient's home as an originating site and allowing virtual visits for new patients in addition to established ones. Before COVID-19, "I could not initiate a telehealth visit with someone I had never met in person for the first time. In Alaska, that included an in-person physical," said Rathkopf. "Those rules were all lifted during the pandemic." As more practitioners started offering telehealth, 46% of US consumers said they were using telehealth in lieu of canceled healthcare visits, up from 11% in 2019, according to McKinsey data that Shih reported at the meeting. More than three quarters of consumers said they would likely use telehealth after the pandemic. Of 297 patients who used telehealth services at Emory Allergy Clinic between March 24 and May 29, 2020, 88% of them rated their comfort level on seeing a doctor virtually with the highest score (10 out of 10) on a survey published by Shih and colleagues. Forty percent rated their telehealth visit equivalent or superior to a traditional outpatient encounter. And in a consumer survey conducted by Accenture, 64% of patients said they would change practitioners if they couldn't see the doctor via telehealth.

Life-Threatening Paradoxical Bronchospasm May Be Missed in COPD or Asthma

A rare and potentially life-threatening adverse effect of bronchodilator therapy may be overlooked among patients with chronic obstructive pulmonary disease (COPD) or asthma, according to a researcher who reviewed spirometry test results from US military veterans. Nearly 1.5% of the tests met the criteria for paradoxical bronchospasm, which refers to airway constriction that may rapidly occur after inhalation of a short-acting beta2 agonist (SABA) such as albuterol. However, none of those reports alluded to paradoxical bronchospasm, said investigator Malvika Kaul, MD, fellow in the department of pulmonary and critical care at the University of Illinois at Chicago and the Jesse Brown Veterans Affairs Medical Center, also in Chicago. "Paradoxical bronchospasm was neither recognized nor reported in any spirometry test results," Dr Kaul

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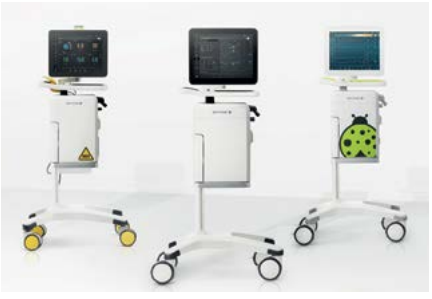

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Retraction: Using Simulation-based Mastery Learning to Teach Residents to Manage Mechanical Ventilators

We are retracting an article that was published in our Winter 2022 issue: "Using Simulation-based Mastery Learning to Teach Residents to Manage Mechanical Ventilators," (the article has been removed from the online issue).

We removed the article after the American Thoracic Society, publisher of the journal *ATS Scholar* (https://www.atsjournals.org/journal/ats-scholar), informed us that extensive sections of the article had been reprinted without permission from the *ATS Scholar* article "Impact of Simulation-based Mastery Learning on Resident Skill Managing Mechanical Ventilators" by Clara J. Schroedl, Alexandra Frogameni, Jeffrey H. Barsuk, Elaine R. Cohen, Lakshmi Sivarajan, and Diane B. Wayne (*ATS Scholar* 2020;2[1]:34-48, https://dx.doi.org/10.34197/ats-scholar.2020-0023OC).

The *ATS Scholar* article was published under a Creative Commons Attribution Non-Commercial No Derivatives License 4.0, an open access license that does not permit commercial reuse of content without permission. In addition, although a previous conference abstract version of the article (https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2018.197.1_MeetingAbstracts.A6299)was included in the reference section, the reference to the *ATS Scholar* article had been omitted.

Respiratory Therapy apologizes to the authors of the *ATS Scholar* article and to the journal.

said in an online poster presentation at the annual meeting of the American College of Chest Physicians, held virtually this year. By recognizing paradoxical bronchospasm, health care providers could address its clinical implications and identify potential alternative management options, according to Dr Kaul. "We hope in the future, education of clinicians about this phenomena is emphasized," Dr Kaul said in her presentation. In an interview, Dr Kaul said she began researching paradoxical bronchospasm after encountering a patient who had an acute reaction to albuterol during a pulmonary function test. "I was not taught about it, and I wasn't recognizing that pattern very frequently in my patients," she said. Prescribing information for Food and Drug Administration–approved SABAs include a warning that life-threatening paradoxical bronchospasm may occur, said Dr Kaul. If paradoxical bronchospasm occurs, the patient should discontinue the medication immediately and start on alternative therapy, according to the available prescribing information for albuterol sulfate. Paradoxical bronchospasm has been linked to worsened respiratory outcomes, including more frequent exacerbations, in patients with obstructive lung diseases, according to Dr Kaul. Two previous large studies pegged the prevalence of paradoxical bronchospasm at around 4.5% in patients with COPD or asthma, but "it has not been reported or addressed in high-risk population, such as veterans who have high prevalence of obstructive lung diseases like COPD," Dr Kaul said.

Researchers Team Up to Study COVID-19 Impact on Lung Function

Boehringer Ingelheim announced that the first patient has enrolled in a new clinical study to observe whether COVID-19 patients with respiratory failure are more susceptible to developing progressive Interstitial Lung Disease (ILD), or scarring of the lungs. Weill Cornell Medicine and NewYork-Presbyterian Hospital are leading the clinical trial. "There is increasing evidence that respiratory failure observed in COVID-19 infected patients leads to a progressive form of Interstitial Lung Disease," said Rob Kaner[1], M.D., principal investigator, associate professor of clinical Medicine and of Genetic Medicine and director of the Interstitial Lung Disease Program at Weill Cornell Medicine in New York, and a pulmonologist at NewYork-Presbyterian/Weill Cornell Medical Center. "This prospective study will define the incidence of progressive ILD in the COVID-19 patient population and investigate if there are specific biomarkers that may identify patients at risk for progression." The study, NCT05074875, is a 48-week observational, prospective registry study that will enroll an estimated 300 patients who were hospitalized with hypoxemic (below normal oxygen levels) respiratory failure associated with COVID-19 at Weill Cornell Medicine and NewYork-Presbyterian Hospital, and three other medical centers. The primary endpoint of the study is the change in fibrotic and non-fibrotic interstitial opacities on chest HRCT at 48 weeks after hospitalization for COVID-19 or outpatient COVID-19 infections which require treatment with supplemental oxygen. Secondary endpoints include percentage of participants with changes from baseline and evidence of disease progression based on HRCT, relative change in Forced Vital Capacity (FVC) at weeks 12, 24, 48 and 72 among other measures. "This study will help the medical community better understand the prognosis of COVID-19, namely whether a progressive form of ILD and associated biomarkers may occur following respiratory failure in COVID-19 patients," said Craig Conoscenti, M.D., Executive Director/Therapeutic Area Head, Respiratory IPF/ILD, Clinical Development and

Medical Affairs, Boehringer Ingelheim. "It is our hope that this study will take a major step forward in providing treating doctors with new information to better help hospitalized patients affected by respiratory failure due to COVID-19 infection."

Masimo Root with a Multimodal Brain Monitoring Algorithm May Improve Postoperative Neurocognition in Elderly Patients

Masimo announced the findings of a prospective study published in Frontiers in Aging Neuroscience in which Dr Shuyi Yang and colleagues at Capital Medical University in Beijing investigated whether Masimo Root with a multimodal brain monitoring algorithm to manage anesthesia during spinal surgery could improve postoperative cognitive function. In the first study of its kind, the algorithm incorporated measurements from Root, including Masimo SedLine Brain Function Monitoring, Masimo O3® Regional Oximetry, and ANI Analgesia Nociception Index. The researchers concluded that managing anesthesia based on the multimodal algorithm "may improve the post-operative cognitive function and brain function connectivity in elderly patients undergoing spinal surgery compared to routine anesthesia management." Noting that perioperative neurocognitive disorder (PND) is common in elderly patients undergoing surgery, and that PND has been associated with levels of sedation, analgesia, and cerebral oxygen saturation, the researchers sought to evaluate whether use of an algorithm designed around related parameters could help improve this population's postoperative neurocognition. They enrolled 26 patients aged ≥ 65 scheduled to undergo spinal surgery and divided them randomly into an intervention group (n=14) and a control group (n=12). In the intervention group, anesthesia was managed using the algorithm, which incorporated Sedline Patient State Index (PSi) and Spectral Edge Frequency (SEF), O3 regional cerebral oxygen saturation (rSO_2), ANI pain index, mean arterial pressure (MAP), end-tidal CO_2 ($P_{ET}CO_2$), hemoglobin (Hb), and temperature. The control group received routine anesthesia management. To evaluate whether the algorithm improved cognitive function, they a) compared the patients' Montreal Cognitive Assessment (MoCA) score before and 7 days after surgery, b) analyzed the amplitude of low-frequency fluctuation (ALFF) and brain functional connectivity (FC) after MRI, c) measured serum C-reactive protein (CRP) and lipopolysaccharide levels, and d) analyzed the correlation between FC and changes in inflammatory marker levels. The researchers found that the mean postoperative MoCA score was higher in the intervention group (24.80 ± 2.09) than in control group (22.56 ± 2.24) ($p = 0.04$), with no significant difference in the incidence of PND between the groups. (The MoCA score was also higher in the intervention group than in the control group preoperatively, but to a lesser degree than postoperatively.) They also found that patients in the intervention group had significantly increased ALFF values in several brain regions after surgery ($p < 0.05$) and enhanced FC between the left hippocampus and several regions ($p < 0.05$), which was negatively correlated with the change in serum CRP (pre- vs. post-intervention) ($r = -0.58$, $p = 0.01$). The authors concluded that "anesthesia management based on multimodal brain monitoring under general anesthesia may improve the postoperative cognitive function and brain function connectivity in elderly patients undergoing spinal surgery compared to routine anesthesia management, as evidenced by increased brain activity (ALFF), enhanced FC, higher MoCA score, and reduced systemic inflammation. The extent of postoperative systemic inflammation was negatively associated with the FC enhancement and may be accompanied by a lower MoCA score. Our findings provide a basis for more effective management of elderly patients who undergo surgery to reduce the risk of cognitive disorders and improve brain function. Michael A.E. Ramsay, MD, FRCA, Chair Emeritus of the Department of Anesthesiology and Pain Management at Baylor University Medical Center, commented, "Postoperative

neurocognitive disorders (PNDs) are commonly seen in elderly patients, and may be very distressing to the patient and family. This small, prospective, randomized clinical study has demonstrated that precision multimodal monitoring of the brain intraoperatively can result in significantly improved mental status of surgical patients postoperatively. The study patients were maintained at a precise depth of anesthesia, cerebral oxygenation, analgesia, and temperature using the Masimo Root monitor. Postoperatively the MoCA score was statistically higher ($p < 0.04$) in the study group and the inflammatory marker levels in the brain were significantly reduced ($p < 0.05$), as well as inflammatory markers systemically ($p < 0.01$). A MoCA score of 25-30 represents normal cognition and 21-24, 10-20, and 9 and below, mild, moderate, and severe cognitive impairment, respectively." Dr Ramsay continued, "This was a well implemented study, and while it may have been small, it has large implications regarding the value of precision monitoring during surgery and with the potential for application in the intensive care unit (ICU). This may represent a vital advance in the prevention of PND and also the prevention of delirium in ICU patients. Larger studies will be needed to confirm these preliminary data." ANI on Masimo Root has not received FDA clearance and is not available for sale in the US.

Ventilator Recall Sparks Changes

The recall of some positive airway pressure devices and mechanical ventilators prompted some researchers to study how to optimize a transition to nonrecalled devices. Researchers with the Division of Pediatric Pulmonology, Department of Pediatrics, Children's Healthcare of Atlanta, Emory University, Atlanta, Georgia, launched a retrospective study of children after a Philips Respironics recall notification issued in June

Continued on page 24…

SPOTLIGHT ON VENTILATION

Breas

Responses provided by Chris Southerland, General Manager US and Canada, Commercial Operations

What ventilation products does your company offer?

Vivo Life Support Ventilation

The ultra-portable Vivo 45 LS life support ventilator is designed to maximize independence and mobility to the patient thanks to its ultra-small footprint, comfortable eSync trigger technology and quiet operation. Intended for both adult and pediatric patients. Additionally, the Vivo 45 LS has capabilities for integrated SpO_2, $EtCO_2$, and FiO_2 monitoring solutions, reducing the need for additional devices.

The Vivo 45 LS is FDA 510(k) cleared for adults and pediatric patients who weigh 11 lbs / 5 kg or more, however, the mouthpiece ventilation modes are for adult patients only.

The Vivo 65, an advanced life support ventilator combines clinical excellence, connectivity and monitoring possibilities for both pediatric (greater than 11 lbs / 5 kg) and adult patients in hospitals, post-acute care institutions and the home. It delivers true clinical excellence thanks to its accurate volume delivery and highly responsive trigger system. Additionally, the Vivo 65 has capabilities for integrated SpO_2, $EtCO_2$, and FiO_2 monitoring solutions, reducing the need for additional devices.

EveryWare Cloud Connectivity Solution

At Breas, we know that aging populations and modern lifestyles can lead to healthcare access, resources and budgets being stretched to crisis point. Patients with chronic respiratory conditions compound the situation often requiring multi-disciplinary teams and support mechanisms to manage them effectively.

Remote technology has the opportunity to not only enhance patient's quality of life and make their treatment more effective, but also help plan interactions with patients more effectively, cutting out needless and inconvenient traveling.

By enabling the provision of care outside of the hospital, the aim of EveryWare is to help make a more productive use of healthcare resources and reduce expensive secondary care admissions.

What are the new features?

Breas is constantly innovating and adding new features and functionality to both our devices and cloud based connectivity solutions. We urge anyone interested in seeing the latest clinical and operational enhancements to contact your local Breas sales representative for a presentation or demonstration.

Tell us about your company's current or recent R&D efforts.

Again, Breas recognizes that innovation coupled with providing the highest quality of devices must be the focus in everything we do. Breas is working closely with industry to enhance clinical and operational capabilities of the Vivo 45 LS and Vivo 65. Breas market research aligned with clinical and operational needs of the industry will provide R&D enhancements that will keep the Vivo relevant for many years to come.

Discuss the training and support services you offer.

Breas is focused on providing superior clinical and operational training and support. We recognize that clinical RT staff and service repair staff turnover can complicate a providers' ability to maintain consistent training and support for your staff. Breas offers on-site clinical training by our staff of RT's at no charge as well as several webinar based CE programs throughout the year. Breas also has Education by Breas as a core on-line educational function along with partnering with the Ventilator Training Alliance where tutorial videos are posted for Vivo devices. Breas also offers both virtual and on-site service training for our customers and service center partners.

Where are your products used? (ie, hospital, home, etc.)

The Vivo 45 LS and Vivo 65 are classified as life support ventilators, so our marketing and sales efforts are predominantly in home care as well as LTC facilities and acute facilities with transitional care departments.

What developments do you foresee for ventilation products and applications?

In the medical device world, regardless of the therapeutic application, there seems to be a push for innovation related to 1) Portability = smaller, lighter, longer battery life; 2) Clinical utility = one device covering early to late-stage disease progression; 3) Connectivity; 4) Total cost of ownership. The Breas Vivo 45 LS is recognized as a leader in these innovation categories, and Breas will be working hard in the near future

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[1] Huynh TT, Liesching TN, Cereda M, Lei Y, Frazer MJ, Nahouraii MR, Diette GB, Efficacy of Oscillation and Lung Expansion in Reducing Postoperative Pulmonary Complication, Journal of the American College of Surgeons (2019)

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to continue to expand this device to provide more clinical and operational utility for our provider customers and their patients.

Getinge

Responses provided by Eric Honroth, President, North America

What ventilation products does your company offer?
Our Servo family of ventilators is tailored to the acute care segment. No two patients have the same challenges, which is why we have developed a broad portfolio of ventilators and tools that let you personalize the treatment for lung protection and faster weaning. Servo-u, Servo-n, and Servo-u MR ventilators give clinicians many options for personalized lung protection and weaning. To round out our product portfolio, we also offer the Servo-air, a powerful turbine-driven ventilator independent of wall gas, along with battery backup making it perfect for intra-hospital transport. It can be easily lifted and moved with patients within the facility and is excellent as a stepdown unit or for intermediate care.

What are the new features?
We constantly strive to innovate our products and advance the markets that we serve. By providing upgrades and updates to our Servo family of ventilators, we ensure they can be customized to support the changing needs of users over the lifetime of the ventilator. In April of 2021, we received FDA 510(k) clearance for software 4.1. With this software upgrade for the Servo-u and Servo-n combined, we added several new functionalities and options across all patient categories—adult, pediatric and neonatal. We broadened our portfolio of lung-protective tools, including the Automatic Stepwise Recruitment Maneuver (Auto SRM), a standardized and automated workflow that guides lung recruitment and helps clinicians identify a personalized PEEP that provides the lowest driving pressure, a variable strongly associated with patient survival in ARDS. Stress index and Transpulmonary pressure monitoring, including key parameters for assessment of lung stress during controlled and spontaneous ventilation, complements the lung protective toolkit, which was designed to optimally divide the cognitive workload between the clinician and the ventilator. Additionally, the clearance includes Heliox therapy. This helps reduce the work of breathing of patients suffering from obstructive lung diseases. In addition to 4.1, we offer NAVA (Neurally Adjusted Ventilatory Assist) and Edi monitoring as part of the Servo portfolio (Servo-u/n) focusing on the activation of the diaphragm and protection of the lungs.

We have also introduced the Servo-u MR to the US market, complementing the Servo Family, expanding Getinge's platform of ventilators into the MRI room. Designed to guide the ventilator into a safe position, the Servo-u MR includes a magnetic field indicator with visual and audible alerts and an auto-lock handle that locks all four wheels as soon as the clinician releases the ventilator. These products join NAVA® and Edi monitoring as part of the Servo portfolio focusing on the activation of the diaphragm and protection of the lungs.

Tell us about your company's current or recent R&D efforts.
Getinge is one of the market leaders in mechanical ventilation. For over 50 years we have collaborated with intensive care clinicians worldwide, and continue to work together to develop ways to improve the software offerings of the Servo ventilators. Getinge has a history of firsts for the acute care market in terms of personalized ventilation treatment including our NAVA technology. We are constantly innovating our products and solutions and continuously looking to enhance patient care.

Discuss the training and support services you offer.
Getinge's main priority is to ensure that we help save and improve as many lives as possible and keep our employees and our clinicians safe and healthy. This philosophy is consistent with our brand promise: Passion for Life. We go beyond the product to provide tools and support in-person or virtually, across multiple areas of the business. We offer the Getinge Institute, our online training portal, for easy access to on demand education. Customers also have access to Getinge Care, our Service program, which includes access to original consumables and spare parts, scheduled maintenance, training, e-learning, and online availability of resources.

At the start of the pandemic, we launched the COVID-19 resource center—a dedicated section on getinge.com to provide guidance on how to get the most from our offerings in treating patients as well as other practical information and advice. Getinge also started the Ventilation Training Alliance, in conjunction with Allego, to deliver on an essential need for clinicians. VTA offers a free app to medical professionals, which provides a library of training and product resources.

What developments do you foresee for ventilation products and applications?
If COVID has taught us anything, the world has changed around digital applications and we are exploring what that world could look like. Our mission will always be to further advance the lung and diaphragm protective strategies for better patient outcomes.

SPOTLIGHT ON BLOOD GAS

Masimo

Tell us about your oximetry products currently available.
We offer a wide range of pulse oximetry products, including both continuous and spot-check monitoring solutions with Masimo SET® pulse oximetry.

Over 30 years ago, Masimo founder and CEO Joe Kiani was convinced that the use of adaptive signal processing could solve the long-time patient monitoring concerns clinicians faced by separating true arterial signal from sources of noise. With this insight, Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry was born—empowering clinicians with accurate, real-time patient oxygenation data even during periods of motion and low perfusion.

Masimo SET® pulse oximetry is available on various monitoring devices, including the Radical-7® Pulse CO-Oximeter® and the Rad-67™ Pulse CO-Oximeter. Radical-7 is a continuous monitoring solution designed to provide a variety of important patient parameters in a versatile, upgradeable monitor—for handheld use, use at the bedside, or during transport. For monitoring on the go, the Rad-67 spot-check monitoring device provides noninvasive total hemoglobin and SET® pulse oximetry in a light, handheld format. With its intuitive touchscreen

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- Auto-Rate factors in both the patient's actual respiratory rate and their minute ventilation averages over the night for support only when necessary.

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and fast, on-demand results, Rad-67 makes an ideal mobile monitoring solution in clinical and non-clinical settings, such as emergency rooms, pre- and post-surgery settings, and physician offices. SET® can also be integrated into third-party monitors. For use with these devices, we offer a variety of sensors designed for patient comfort and ease of use, including RD SET® sensors and specialty sensors.

In clinical settings, Masimo SET® has demonstrated fewer false alarms and more true alarms than conventional pulse oximeters,[1] and over 100 studies have shown that SET® outperforms other pulse oximetry technologies.[2] At Masimo, we never put innovation on hold—and our proven SET® technology is no exception. We are excited to announce a significant improvement in our SpO2 accuracy specification with the latest RD SET sensors, from 3% to 1.5% ARMS during motion, in all patient populations.

Today, Masimo SET® is estimated to be used on more than 100 million patients in leading hospitals and other healthcare settings around the world and is the primary pulse oximetry at 9 of the top 10 hospitals according to the 2019-20 *US News and World Report* Best Hospitals Honor Roll.

Discuss the range of your oximetry products' applications.
Our pulse oximetry solutions are versatile, customizable, and transportable. Whether it's continuous pulse oximetry monitoring in critical care areas or spot-check patient monitoring during vital signs checking, SET® technology can be used anywhere pulse oximetry is needed—in pre-hospital, acute, and post-acute care settings.

Designed for a variety of clinical scenarios, we offer RD SET sensors for all patient populations as well as specialty sensors, which are designed specifically to meet the needs of trauma, neonatal, infant, and pediatric patients.

To date, several studies have demonstrated the clinical benefits of Masimo SET® across various care areas.[2] For example, when Masimo SET® was coupled with changes in clinical practice, it led to a significant reduction in rates of severe retinopathy of prematurity (ROP).[3] Additionally, in a study of 122,738 infants, critical congenital heart disease (CCHD) screening sensitivity increased from 77% to 93% with the combined use of Masimo SET® and clinical assessment.[4]

Alongside SET® pulse oximetry, offering SpO2, pulse rate, and perfusion index, advanced Masimo rainbow® measurements enable clinicians to gain an array of additional insights into patient status in real time. These noninvasive measurements include pleth variability index (PVi®), total hemoglobin (SpHb®), carboxyhemoglobin (SpCO®), methemoglobin (SpMet®), oxygen content (SpOC™), and acoustic respiration rate (RRa®). With more information at their fingertips, clinicians can make better informed care decisions.

We help clinicians manage this important patient data with the Root® Patient Monitoring and Connectivity Platform. Root's advanced connectivity capabilities aggregate and display data from other Masimo and even third-party devices. With the assistance of Masimo Iris Gateway® or Patient SafetyNet™, that data can be automatically transferred into hospital electronic medical records (EMRs) and displayed at central view stations and on UniView™, which intelligently visualizes data and alarms to help reduce cognitive overload and streamline care team workflows. Root is compatible with both third-party devices and our expanded portfolio of noninvasive monitoring technologies and devices, which includes brain monitoring (Next Generation SedLine® and O3® Regional Oximetry) and ventilation monitoring solutions (NomoLine® Capnography and rainbow Acoustic Monitoring®).

What oximetry products do you have in development?
At Masimo, we're always looking for new and innovative ways to help improve patient outcomes through advanced monitoring technologies and systems. It is also our goal to help provide clinicians with the tools they need to better manage the data generated by our technologies—freeing them up to spend more time delivering bedside care.

Recently, we released the Radius PPG™ tetherless pulse oximetry solution in the US and plan to release it globally in the future. Radius PPG provides continuous SET® pulse oximetry monitoring without the need for a cabled connection to a monitor.

Lightweight and comfortable to wear, Radius PPG gives patients freedom of movement without compromising safety—providing uninterrupted continuous pulse oximetry monitoring no matter where they go. It's easy to pair Radius PPG with other Masimo products and third-party devices.

What type of customer assistance and training do you offer?
Masimo takes pride in offering the best education solutions for customers. Expert clinical specialists, including trained nurses and respiratory therapists, work hand-in-hand with the hospital's clinical educator(s) to build an education plan that meets the needs of hospital staff.

To help clinicians maximize the utility of our products, we've created three phases of customer training—modeled after Adult Learning Theory—that provide engaging, effective educational content. These phases include self-directed eLearning via our learning portal (MasimoU), on-site demonstration, and "super-user" training geared toward in-house clinical champions in various care areas. Through these trainings, customers learn the fundamentals of pulse oximetry, SET® technology, key physiological and laboratory concepts, advanced troubleshooting, proper sensor placement, and much more.

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SPOTLIGHT ON SPIROMETRY

MGC

CPFS/D USB Spirometer

When you need full-function spirometry and space is at a premium, the CPFS/D USB spirometer from MGC Diagnostics is a most fitting solution. This small, portable system is packed with technological advances and features to meet all your testing and data management needs. The CPFS/D USB spirometer is compatible with desktop and laptop computers for maximum flexibility. It has incentive graphs for spirometry, which are ideal for pediatric populations. Powered by our Ascent cardiorespiratory diagnostic software, you can be assured it will do more than meet your testing and data management needs. MGC Diagnostics utilizes the preVent flow sensor with the CPFS/D USB. This gives maximum infection control when used with a pulmonary function filter, cleaned between uses, or discarded. One flow sensor- one technology—one solution.

GoSpiro Spirometer

The GoSpiro spirometer is the first spirometer designed for connected health applications and remote patient monitoring. This device provides diagnostic quality test results and delivers spirometry data that is reimbursable and able to be conducted at home or in a clinic.

The GoSpiro spirometer transmits the data to the MTI CarePortal™, a comprehensive and customizable cloud-based information portal designed for healthcare providers. The GoSpiro is just one of several interfaced devices the MTI CarePortal can receive real-time data from including the GoECG, GoWalk, pulse oximetry, blood pressure, glucose, weight, temperature, FeNO, FOT, hand dynamometer and the Biovotion monitor.

Ideal for Remote Patient Monitoring, the GoSpiro Spirometer is the only spirometer to have an Avatar enabled coach that walks patients unfamiliar with performing spirometry through the process and provides post-test comments to guide patients to optimal performance.

Vitalograph

The Vitalograph new Pneumotrac spirometer equipped with new Spirotrac®6 is the most advanced, accurate, and durable spirometer available. Not only is testing simple with a click of the space bar, but the software is nimble enough for customizations of workflow, reports, EMR interfacing, and beyond. In addition, the 2019 ATS grading standard is incorporated in Spirotrac®6 and our Bacterial/Viral Filter keep your patients safe from cross contamination from many viruses including the Flu and Covid-19.

The Benefits of Remote Monitoring for Patients with Cystic Fibrosis

Chris Campbell

For most patients who need to be tested with a spirometer, it requires them to visit a controlled hospital setting where the test is conducted by trained medical professionals.

But what if a patient with a condition impacting lung function could do the test themselves from the comfort of their own home?

That's what the Cleveland Clinic has detailed in an article related to its study measuring the efficacy of a home monitoring system for patients with cystic fibrosis (CF) awaiting organ transplant. The study utilized Monitored Therapeutics' (MTI) GoSpiro home spirometer, along with MTI's CarePortal cloud-based remote monitoring solution.

The article, published on its website as one of the clinic's Patient Stories, features the story of Jason Tutoki, a 21-year-old Ohio resident living with cystic fibrosis. After years of going in for spirometry tests, Jason started doing it himself at home in the summer of 2020, using the GoSpiro spirometer.

"It wasn't hard to do," says Jason in the article about using the device. The technology is the first spirometer designed for connected health applications and remote patient monitoring. "It's the exact same machine they use in the hospital. It's just portable."

The Cleveland Clinic study focused on clinical tools including a clickable survey and home measured clinical variables to update a patient's lung allocation score (LAS). In the US, individuals are prioritized for life-saving lung transplant by the (LAS), which considers both the risk of mortality awaiting transplant and the likelihood of survival after transplant.

"A chronic lung disease that gets progressively worse, CF can also affect other organs in the body including the pancreas and, in Jason's case, his liver," writes the article's author. "While the disease was manageable for a few years, Jason has been in and out of the hospital numerous times for more than a decade, as the effects on his health steadily worsened. He has required coordinated care from dozens of specialists, in pediatric and adult pulmonary care, to keep him alive."

The article details how Jason repeatedly suffered from hemoptysis, or coughing up blood from the respiratory tract.

"As the occurrences increased, in frequency and severity, Jason was hospitalized for over a month. Placed in a coma to enable his body to rest, Jason came close to dying on a few occasions." So the need for Jason to receive transplants was dire.

The article quotes Jason as saying the home monitoring system likely accelerated the process of him receiving transplants — two lungs and a liver — after more than a year on a waiting list.

"Patients with CF requiring transplants can move up and down on the list, based on the changing condition of their lungs," writes the article author. "Since patients with CF, who are awaiting transplants typically only visit the hospital for updates quarterly, any change in their condition that could affect their waiting list status can go unnoticed for weeks at a time."

Once a patient like Jason is accepted into the study, respiratory therapists configure the GoSpiro for the patient and train them on how to use it. Patients complete the home testing at least once per week.

Using the MTI CarePortal, physicians receive updates weekly on their patient's condition, with the data being "transmitted automatically after each test is completed. They're alerted if the results worsen significantly," the article says.

The home monitoring study is led by Carli Lehr, MD and has seen dramatic results.

"Remote monitoring provides an essential service," says José Ramos, respiratory therapist at Cleveland Clinic Respiratory Institute, who along with fellow respiratory therapist, Mike Hoffman, have now coordinated home monitoring care for more than 500 post-transplant, and now, pre-transplant patients, the article says. "If a patient's lung (performance) drops during a time when they aren't in the hospital, we know it right away. It may change their (waiting list) score and move them up to get a transplant sooner."

According to the article, an alarm sounds if a patient's lung function results decline, prompting the medical team to take appropriate action.

Chris Campbell is the Senior Editor of Respiratory Therapy.

"At one point, (Jason's) lung function score nosedived, prompting Jason Turowski, MD, associate director of the Adult Cystic Fibrosis Program, to have him undergo further testing," says the article. "Those results confirmed the decline. Jason's Chronic Respiratory Infection Symptom Score (CRISS) was changed accordingly. Now listed as a higher-priority patient on the lung/liver transplant list, Jason learned he was a match for a triple transplant and underwent successful surgery a week later. Since then, despite a few bumps in the road that have required some changes in his anti-rejection medication, Jason is thriving and continues using the remote monitoring system for his new lungs. He's now able to 'run around outside and go on hikes,' the types of activities he could rarely enjoy before."

"Jason's story depicts the excellent multidisciplinary care at Cleveland Clinic. Providers from different specialties came together to treat Jason and improve his health and well-being," says Kaddakal Radhakrishnan, MD, pediatric liver specialist at Cleveland Clinic Children's, in the article.

"It hasn't been easy for Jason, with plenty of bumps in the road. But I'm hopeful he has a long and healthy life ahead."

News…continued from page 16
2021 that affected many of their positive airway pressure devices and mechanical ventilators including the Trilogy 100 and 200 ventilators that are often utilized in children using home positive pressure ventilation via tracheostomy (PPV-T). "Optimal strategies to replace ventilators in children using home PPV-T affected by the Philips recall are unknown," the researchers wrote in their study, entitled "Ventilator change in children on home mechanical ventilation affected by the Philips Respironics trilogy ventilator recall," and published in October 2021. "We conducted a retrospective study of children using home PPV-T with recalled Trilogy ventilators who underwent inpatient ventilator change to non-recalled portable home ventilators (PHV) using our collaborative institutional protocol. During the study period, there were 40 children using PPV-T with recalled Trilogy ventilators and 19 patients underwent inpatient ventilator change either during an elective hospitalization (n = 8) or during an unscheduled or postoperative hospitalization (n = 11). The median duration of hospitalization for ventilator change was 2 days (interquartile range: 6 days) and generally 1 day for patients admitted solely for ventilator change." The 19 patients were changed to either Breas Vivo 65 (Breas Medical AB, n = 13) or AstralTM 150 (ResMed, n = 6) based on ventilator availability with the patient's DME company. According to the study, the recall was due to "problems related to the polyester-based polyurethane sound abatement foam used in the affected devices that could generate particulate matter which may be inhaled or ingested by the user, and off-gas potentially toxic carcinogenic chemicals. In the recall notice, Philips Respironics has reported patient complaints of black particles in the airpath circuit of the devices, cough, upper airway irritation, headache, chest pressure, and sinus infection. Philips Respironics reports potential risks of particulate and chemical exposure due to off-gassing, including irritation of the skin, eye, and respiratory tract, headache, asthma, hypersensitivity, nausea, vomiting, and toxic carcinogenic effects. Although there have been no reported deaths due to these issues, the duration of exposure required to produce symptoms is unknown."

The American Academy of Sleep Medicine, American Thoracic Society, and Canadian Thoracic Society has provided guidance for physicians managing patients affected by the Philips recall. For patients using life-sustaining ventilators, Philips Respironics and professional societies have recommended that patients not stop therapy until after talking to their physician. "This recall has imposed a burden on pediatric clinicians and healthcare systems requiring notification of patients using affected ventilators, reviewing the risks and benefits of continued therapy, triaging children with higher medical acuity for ventilator replacement, and arranging for replacement unaffected ventilators during a summer surge in hospitalizations due to COVID-19 and respiratory infections," the authors write. In the study's discussion section, the authors concluded that while limited by the single institution retrospective study design with a small sample size, a "collaborative approach" can optimize the transition to nonrecalled devices.

"Based on consensus within our pediatric pulmonology division, this institutional protocol was formulated to facilitate and prioritize ventilator transition in children using affected Trilogy ventilators," they write. "Since children using PPV-T are often medically complex and fragile compared to adults, we elected to perform ventilator changes in the inpatient setting where children could be closely monitored and appropriate changes in ventilator settings could be performed, if required.
Continued on page 29…

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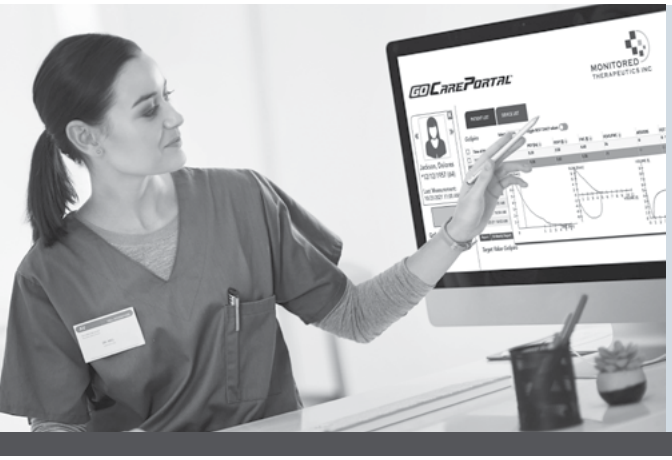

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Dysphagia Following Tracheostomy in the Adult Patient

Carmin Bartow, MS, CCC-SLP, BCS-S

It is well-known that patients with tracheostomy tubes have a high risk of aspiration and associated complications. Normal swallowing occurs with close synchronization of breathing and swallowing, positive airway pressures, and intact airway protection. When a tracheostomy tube is placed, swallow function may be negatively impacted. To identify changes in swallowing, understanding normal swallowing, alterations in swallow physiology related to tracheostomy, and therapeutic techniques to improve swallow safety and efficiency is key. One step following tracheostomy is to close the system and restore more normal functions for swallowing, which may include use of a Passy-Muir® Valve (PMV®).

Normal Swallowing

Swallowing is a pressure-driven event requiring coordination of sensorimotor actions to move food and liquid from the oral cavity to the stomach and to prevent material from entering the airway. The act of swallowing is typically divided into the three phases: oral, pharyngeal, and esophageal.

Oral Phase

The oral phase is often subdivided into the pre-oral, oral preparatory, and oral transit phases. The pre-oral phase initiates the process of swallowing using cognitive, auditory, visual, and olfactory inputs for readiness for accepting food or liquid into the mouth. Next, in the oral preparatory phase of swallowing, food is chewed and manipulated into a cohesive bite (bolus). Lastly, the oral transit phase involves the tongue pushing the bolus toward the back of the mouth.

Pharyngeal Phase

Sensory receptors in the back of the mouth and upper throat (known as the oropharynx) trigger the pharyngeal swallow, which is a rapid, sequential activity occurring within one second. The basic components of the pharyngeal swallow include:

- Soft palate elevation and contraction of the upper throat muscles (called pharyngeal constrictor muscles). This movement blocks food and liquid from entering the nasal cavity.
- Elevation and anterior movement of the hyoid bone and larynx. This movement is necessary to invert the epiglottis for airway protection and to open the muscle at the top of the esophagus (known as the upper esophageal sphincter or cricopharyngeus).
- Airway closure to prevent aspiration which is accomplished by:
  - □ True vocal fold closure and brief cessation of respiration.
  - □ False vocal fold (structures superior to vocal folds) contraction.
  - □ Epiglottic inversion.
- Opening of the upper esophageal sphincter.
- Base of tongue retraction and contraction of the muscles of the pharynx, which is essential for pushing food through the pharynx.

Esophageal Phase

The entry of the bolus through the upper esophageal sphincter initiates the esophageal phase of swallowing. A combination of muscular contraction and relaxation (known as peristalsis) and gravity transfers the bolus through the esophagus, lower esophageal sphincter, and into the stomach.

Breathing and Swallowing Coordination

For normal swallowing to occur, coordination of breathing and swallowing is required. Breathing ceases briefly during the swallow due to the physical closure of the airway as described above and due to sensory and motor brainstem signals. The respiratory pause functions to assist with protecting the lungs from aspiration. An additional protective feature is when swallowing occurs mid-expiration: exhalation — swallowing — exhalation. The post-swallow expiration serves as a protective mechanism to expel any material which may have penetrated the entrance of the airway during swallowing. Conversely, inspiration after the swallow could potentially increase the risk of aspiration as the negative pressure of inhalation has the potential to draw food and liquid residue toward the lungs. The ideal breathing and swallowing coordination has been summarized as "the higher frequency of the expiratory–swallow–expiratory pattern and the physiological advantages support the conclusion of this pattern as the predominant and potentially optimal coordination of these two systems."[1]

Pressures

A closed aerodigestive system allows for normalized swallowing pressures. Normal swallowing pressures include pressure from muscles and structures to move the bolus through the oral cavity and pharynx and subglottic airway pressure. Lung volume and respiratory recoil combine to generate positive sub-glottic

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pressure. This pressure peaks during swallowing when the vocal folds close which creates a buildup of positive pressure below the vocal folds. This pressure may serve as an additional barrier to aspiration. There is also speculation that subglottic pressure is necessary to trigger sensory receptors in the larynx to send messages to the brainstem to further regulate breathing and swallowing coordination.[2-3]

Dysphagia

Dysphagia is the terminology used for a swallowing disorder, which is a disruption in one or more of the processes or protective mechanisms and leads to changes in swallow function. When swallowing impairment occurs, complications such as malnutrition, dehydration, and aspiration pneumonia may arise. Healthcare providers may be able to minimize patients' risk of developing these complications by being watchful and reporting signs and symptoms of aspiration.

Signs and symptoms of dysphagia include:

- Unintentional weight loss.
- Coughing, choking, or throat clearing during or after meals.
- Wet vocal quality.
- Pain with swallowing.
- Sensation of food sticking in throat or chest.
- Fever 30 minutes to one hour after meal.
- Shortness of breath or chest congestion during meals.
- Evidence of aspiration in tracheal secretions.

If signs and symptoms of dysphagia are observed, a referral to the speech-language pathologist (SLP) is warranted. The SLP is responsible for the assessment and treatment of dysphagia and may be able to design a treatment plan to maximize oral nutrition and minimize the risk of aspiration.

Dysphagia Related to Tracheostomy

Aspiration in patients with tracheostomy is reported to occur in 50 – 93% of the patient population with tracheostomies, and of those patients, silent aspiration is reported to occur in up to 82% of them.[4-7] One contributing factor may be the presence of a tracheostomy tube, especially when it is unoccluded and the cuff is inflated. In this condition, the normal closed aerodigestive system is altered. An open aerodigestive system may result in altered mechanics, impaired breathing and swallowing coordination, lack of positive airway pressure, and reduced airway protection. The following have been reported regarding the negative impact of a tracheostomy on swallowing:

- Impaired laryngeal elevation.[8-11]
- Desensitization of the larynx.[8, 9, 12, 13]
- Delayed laryngeal vestibule closure associated with tracheal aspiration.[14]
- Reduced subglottic air pressure.[2,7]
- Disuse atrophy of larynx.[16]
- Decreased coordination of breathing and swallowing.[17]
- Decreased effectiveness to clear secretions from upper airway.[18]

Improvements with the Passy-Muir Valve

The Passy-Muir Valve is a bias-closed position, no-leak valve that redirects airflow around the tracheostomy tube and up through the vocal folds, mouth, and nose. Use of the Valve allows the patient to create positive airway pressure and restores the patient to a more normal closed respiratory system. The restoration of airflow through the upper airway and positive airway pressure has numerous clinical benefits including improved voice, secretion management, cough effectiveness, and swallowing ability.

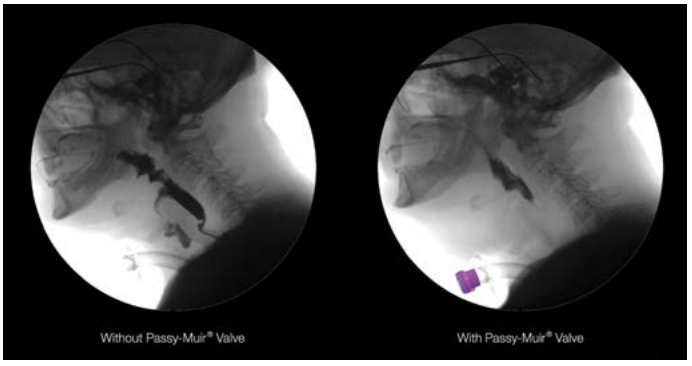

Figure 1. Closing the system with a Passy-Muir Valve restores pressure: positive pressure = positive outcomes.

Subglottic Pressure

Gross et al. (2003) investigated the impact of subglottic pressure on swallowing physiology in patients with a tracheostomy tube.[15] They found that when the Passy-Muir Valve was on, patients demonstrated less aspiration and faster movement of the bolus through the pharynx as compared to an open tracheostomy tube. Studies have shown that swallowing physiology is measurably different in the absence of upper airflow and subglottic air pressure as seen with an open tracheostomy tube as compared to the closed tube condition when using a PMV.[7,15]

Breathing and Swallowing Coordination

Prigent et al. (2011) investigated the effect of a Passy-Muir Valve on breathing-swallowing interactions.[17] They found that expiratory flow towards the upper airway after swallowing was negligible without the PMV in place and was restored when using the PMV.

Airway Protection

One issue that occurs with a tracheostomy is that an open tube reduces the functions that assist with airway protection, such as reduced pressure, hyolaryngeal excursion, and sensation. However, research has shown that closing the system improves these functions. Blumenfeld et al. (2011) investigated swallowing function in patients with and without a PMV.[19] Patients were randomized into either a Passy-Muir Valve experimental group or a tracheostomy tube only control group. All patients underwent identical swallowing therapy. The authors reported less aspiration and improvements in secretion management in the group with the PMV. They attributed this improvement to the use of the PMV to close the system, thereby restoring sensation and pressure which protected the airway. Suiter et al. (2003) studied the effects of cuff deflation and PMV placement on swallow physiology.[20] They reported that Valve placement significantly reduced airway penetration and aspiration with liquids. Elpern et al. (2000) also studied the effect of the Passy-Muir Valve on occurrences of aspiration.[21] They found aspiration to be significantly less frequent with the PMV on as compared to swallowing with no Valve. These studies attributed the improved airway protection to the closed system with the PMV in place, restoring various functions involved in airway protection. O'Connor et al. (2019) conducted a systematic review to investigate the physiological and clinical outcomes associated with use of the PMV.[22] Results from their systematic review indicated that research has found that improved secretion

management and reduced aspiration occurs with use of the Passy-Muir Valve.

Additional swallowing intervention

In addition to use of the PMV to aid swallow function, the speech-language pathologist (SLP) may implement compensatory strategies and rehabilitative swallowing therapy. Therapy recommendations are individualized and are typically based on the findings from an instrumental swallowing assessment, such as the Videofluoroscopic Swallowing Study (VFSS) or Fiberoptic Endoscopic Evaluation of Swallowing (FEES®). The plan for intervention is developed and prescribed for an individual patient, involving thorough review of the patient's history, diagnosis, and physiologic changes identified during assessment. Therapy may include any of the following:

- Compensatory strategies
  - □ Postural head, neck, & body changes to improve airway protection or bolus flow.
    - ○ Head turn, chin tuck, head tilt
  - □ Therapeutic maneuvers to reduce aspiration risk and improve bolus flow.
    - ○ Alternating liquids and solids, multiple swallows per bolus
  - □ Diet modification.
    - ○ Altering food and liquid textures to reduce aspiration risk and improve bolus flow, such as the use of thickened liquids or soft foods
- Rehabilitative exercises
  - □ Planned, structured, and repetitive physical activities for the purpose of improving flexibility, strength, and speed, of specific muscles or muscle groups for a specific purpose, including improving endurance.
  - □ For dysphagia, this includes targeted exercises to improve the physiology of swallowing.

Oral hygiene

Another important strategy for dysphagia management includes oral hygiene. Aspiration of saliva, food, or liquid that is colonized with oral bacteria increases the risk of developing pneumonia. Since patients with tracheostomy are at high risk of aspiration, oral hygiene is of utmost importance.

Summary

Individualized and evidence-based dysphagia intervention is necessary to maximize swallowing function and minimize the risk of aspiration in patients with tracheostomy. A combination of compensatory techniques, rehabilitative swallowing therapy, and use of the Passy-Muir Valve may be used to address swallowing dysfunction. Healthcare providers can assist patients with dysphagia by:

- Working closely with the SLP.
- Advocating for early use of the Passy-Muir Valve.
- Advocating for early swallowing assessments.
- Performing oral care before meals.
- Watching for signs and symptoms of aspiration and reporting them.
- Helping patients adhere to dysphagia recommendations established by the SLP.

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A study on bench evaluation of PHVs showed wide variability in performance and triggering sensitivity that may influence assisted ventilation delivery. Moreover, the inpatient setting also permitted parental caregivers' training on using their new non-recalled PHV. Patients who were already hospitalized, scheduled for an elective postoperative hospitalization, or reported symptoms listed in the Philips Respironics recall statement were prioritized for inpatient ventilator change. Our ventilator change protocol relied heavily on patient-centered shared decision-making balancing the risks and benefits of using the recalled Trilogy ventilator and hospitalization to change ventilators. Moreover, close communication and collaboration with the parental caregivers, regional DME companies, hospital bed availability, outpatient and inpatient pulmonologists, and nurse coordinators were key aspects of our protocol. Some obstacles we encountered while implementing our protocol included intermittent shortages of PHVs with the DME companies that also had to service regional adult hospitals. Therefore, we obtained a weekly inventory of available non-recalled PHVs from the DME companies to schedule hospitalizations and PHV changes for our patients. Another challenge was unavailability of inpatient beds due to surges in COVID-19 and other respiratory infections requiring hospitalization during the study period. Therefore, we prioritized ventilator changes in patients who were already hospitalized and hospitalizations for elective ventilator changes were scheduled when beds became available. Although the ventilator change was accomplished during a brief hospitalization in this study, we acknowledge that some parental caregivers may require additional time for ventilator training."

Masimo Launches Dual SET Pulse Oximetry

Masimo announced Dual SET Pulse Oximetry for Root, a highly versatile patient monitoring and connectivity hub. The first application of Dual SET Oximetry is a significant advancement to Masimo SET-guided critical congenital heart disease (CCHD) screening, with the CE marking and European launch of the Masimo SET MOC-9 module and the addition of the Eve CCHD Newborn Screening Application for Root. Together, this combined solution enhances the automation of newborn screenings using Dual SET Oximetry: two simultaneous measurements of oxygen saturation (SpO_2) at pre- and post-ductal sites by the intuitive Eve application, customized to align with a hospital's CCHD screening protocol. CCHD affects approximately 2.5 to 3 newborns per 1000 live births and requires intervention soon after birth to prevent significant morbidity or mortality; later detection in infants also increases the risk of brain damage. Traditionally, newborns were observed for evidence of CCHD by physical assessment and monitoring for common symptoms, but studies have shown that physical assessment of newborns alone can be unreliable and may fail to detect some infants with CCHD before discharge. Adding screening with pulse oximetry can help clinicians identify CCHD before an infant becomes symptomatic. Clinically proven Masimo SET Measure-through Motion and Low Perfusion pulse oximetry has been shown in more than 10 CCHD screening studies—representing over 300,000 babies—to increase the effectiveness of screening newborns for CCHD. For example, in a study of almost 40,000 infants, CCHD screening sensitivity increased from 63% with physical exam alone to 83% with physical exam and SET. In another study of more than 120,000
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Spirometry Standards – The Forgotten Aspects

Ralph Cook

In 2019 the American Thoracic Society (ATS) and the European Respiratory Society (ERS) released a new technical statement on Standardization of Spirometry.[1] These guidelines are an update to the standards last released in 2005 and build upon the foundation of those previous standards. With changes in technology and software capabilities, the standards were updated "to take full advantage of current technical capabilities and evolving best practices."

The standards state that spirometry is the most common pulmonary function test. But there are a couple of aspects of the standards that sometimes are overlooked or understated; the first being the operator performing the spirometry testing. Many times, we refer to testing as "simple" spirometry. If you look at the standards, spirometry is far from simple and not everyone who is performing spirometry testing have the qualifications to do so. Blow into any spirometry device and you get results; however, if the technologist does not fully understand the standards and know how to get the best from their subject, the values obtained could be nothing more than meaningless numbers. Most spirometry software can tell you if an effort is acceptable or repeatable, but that doesn't mean that is the best the subject can do. And what do you do if the subject does not meet these criteria?

Sometimes facilities purchase spirometers and think that once they have mastered the button pushing aspect of the device, they are all set to perform quality testing. Or the main laboratory technologist is trained and proficient in spirometry, and then is given a half hour to train a dozen therapists and nurses to perform testing in the off hours or out on the wards. This does a disservice to the patient as well as lead to a potential misdiagnosis. With the interpreting physician sometimes never seeing the actual patient and only the final report, they trust that the numbers and graphs given to them are quality test results. The numbers obtained may not match the patient's clinical symptoms and the operator may be unaware of that fact. If the operator is not motivated, experienced, or properly trained, the impact on those results can be dramatic.

A 1998 study[2] at a major hospital showed that only 15% of the spirometry tests performed at bedside, outside the main PF lab, met the then spirometry standards for acceptability and repeatability. These tests were performed by a larger group of respiratory therapists. After implementing a quality improvement program that included training, review and limiting the number of people performing spirometry, the percent of tests meeting the ATS standards increased significantly.

Another study[3] from 1999 showed that in practices where the operators had no training, only 3.4% of patients had three acceptable efforts with reproducible results, and only 13.5% of patients met the standards when the operators received minimal training.

Clinicians want to perform quality testing; however, many times they are not given the time or proper training before handed a device and told to test patients. Without someone experienced showing them the proper techniques, reviewing their work, and having the appropriate follow-up, simple spirometry may yield inaccurate and inappropriate results. That is one of the reasons MGC Diagnostics leads the way in sponsoring educational lectures at the state and national level, as well as presenting seminars and webinars on cardiopulmonary diagnostics. Having operators with the right tools helps ensure the best quality testing is obtained from any device, regardless of the manufacturer.

Another aspect often overlooked is the calibration/verification of your device. Some systems on the market, especially handheld models state they are precalibrated or do not require calibration. Advances in technology have allowed us to do this; however, this may lead operators to think they don't need a 3 liter calibration syringe any more. The 2019 ATS/ERS Technical Statement still requires daily verification of the unit. Even devices with disposable flow sensors must be tested each day using a new flow sensor. The devices from MGC Diagnostics with Ascent software do not mandate a daily calibration, but do require a daily verification before allowing you to proceed with testing.

The guidelines differentiate between calibration and verification. Calibration adjusts the transducer signals if needed, while verification validates that you are measuring the correct volume. As part of a Quality Assurance program for your lab, daily verification helps assure your system is operating properly.

The daily verification process is very similar to calibration and means that a 3 liter syringe is connected to the system and "cycled at least three times to give a range of flows varying between 0.5 and 12 L/s (with 3-L injection times between 0.5 and 6 s)". Because spirometry covers a large range of flows, it is

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necessary to perform verification at these flow rates. While the spirometer may give excellent results at the low flows, that does not assure that high flows are accurate. The acceptable tolerance at each flow rate is ±3% (±2.5% for the system plus ±0.5% for the syringe). By using the verification process you are documenting that the system is linear and accurate across all flow rates.

Of course, the subject being tested is the unknown factor in any diagnostic test. However, having technologists who are knowledgeable and experienced in spirometry testing as well as hardware that is accurate and meets the standards will help obtain quality results that will lead to an accurate diagnosis and treatment plan.

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infants — the largest CCHD screening study to date — combined use of clinical assessment and SET increased screening sensitivity from 77% to 93%. Evidence from CCHD studies using SET has even been used to help establish CCHD screening guidelines used around the world. Powered by Masimo SET pulse oximetry, the Eve CCHD Newborn Screening Application is designed to simplify the CCHD screening process by providing step-by-step visual instructions, animations, and a detailed, easy-to-interpret display of screening results — standardizing and enhancing clinical workflows, improving consistency in screening practices among clinicians, and reducing the possibility of calculation errors. Eve also allows clinicians to incorporate perfusion index into screening, which has been shown to increase sensitivity to the detection of CCHD. Already available for Radical-7 and Rad-97 Pulse CO-Oximeters, Eve is particularly well suited for display on Root's large, high-resolution screen. With its built-in barcode scanner, Root can automatically associate patients with their screening results, and with its integration into the Masimo Hospital Automation platform, Root automates the transfer of those results to electronic medical records (EMRs) — eliminating the need for manual charting. Now, with the addition of the new Masimo SET MOC-9 module for Root — made possible by another key differentiator of the hub, its advanced, flexible connectivity capabilities — CCHD screening guided by Eve is even more streamlined and efficient: one pulse oximetry sensor can be connected to Root via Radical-7, and a second via the MOC-9 module, allowing for the pre- and post-ductal SpO_2 readings needed for screening to be taken simultaneously rather than sequentially, with results conveniently displayed on one screen. This Dual SET Oximetry technique streamlines the CCHD screening process, improving clinical workflows. Gerard R. Martin, MD, C.R. Beyda Professor of Cardiology at Children's National Hospital, said, "As an advocate for congenital heart disease efforts nationally and internationally, I believe Masimo SET pulse oximetry is an excellent tool for pulse oximetry CCHD screening. Having access to accurate simultaneous pre-ductal and post-ductal measurements helps simplify the process of screening and allows for rapid recognition of discrepancies, ultimately improving newborn care." Root is a powerful, expandable hub that integrates an array of technologies, devices, and systems to provide centralized, multimodal monitoring and connectivity solutions. Root's plug-and-play expansion capabilities allow clinicians to simultaneously monitor with numerous measurements in addition to dual oximetry Masimo SET, such as advanced rainbow Pulse CO-Oximetry measurements, O3 regional oximetry, and SedLine brain function monitoring, for expanded visibility of patient status. Using Root in combination with the Hospital Automation platform, monitoring data from all connected devices can be automatically charted in EMRs. Augusto Sola, MD, Vice President of Medical Affairs at Masimo, commented, "As a neonatologist who has worked nationally and internationally in the early diagnosis and treatment of hypoxemic and hyperoxemic conditions that affect neonates in order to improve neonatal survival and quality of life for these fragile infants, I know that Masimo SET measure-through motion technology's accuracy and reliability have not only enabled CCHD screening with pulse oximetry, but have helped dramatically reduce retinopathy of prematurity (ROP). SET provides reliable, high-quality monitoring to prevent serious long-term morbidities and is now the standard of care for CCHD newborn screenings and ROP. With the availability of the SET

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4 Reasons to Rethink High-flow Oxygen Therapy

Kathleen Fallon, RRT

COVID-19 has driven clinicians to rapidly change common care processes and practices in an effort to battle this previously unknown pathogen. It has also resulted in new breakthroughs in the treatment of patients in respiratory distress.

During the course of the pandemic, clinicians at the University of Chicago Medicine have observed that oxygen therapy via high-flow nasal cannula (HFNc) therapy can be effective in avoiding mechanical ventilation and endotracheal intubation and can help avoid the need for intubation in SARS-CoV-2 patients.[1]

Clinicians in University of Chicago Medicine's emergency room administered oxygen via HFNC to dozens of COVID-19 patients suffering from respiratory distress with positive outcomes across the board. Only one patient required subsequent intubation. Overall, they avoided mechanical ventilation on 40% of patients and extubated 50% of those who had been on ventilators.[2]

Dräger HI-Flow Star System © Drägerwerk AG & Co. KGaA

What's next for HFNC?

While O2 therapy via HFNC was in use prior to the pandemic, it had been limited to very specific situations, such as the treatment of hypoxemia, asthma and bronchiolitis in infants and pediatric patients.

Now that use of HFNC has been widely used to treat COVID-19 patients, we are experiencing an expansion of therapeutic indications for this oxygen delivery modality.

Kathleen Fallon RRT is a Senior Marketing Manager, Hospital Accessories and Consumables, Dräger.

In April 2021, the American College of Physicians (ACP) released a new Clinical Guideline with recommendations for the appropriate use of oxygen therapy via HFNC in hospitalized patients, citing the benefits of HFNC compared to conventional oxygen therapy (COT) and high-flow systems and noninvasive ventilation (NIV).

The ACP noted, "The purported benefits of [HFNC] compared to conventional oxygen therapy (COT) and high-flow systems and noninvasive ventilation (NIV) include improved patient comfort, compliance and physiological advantages," adding how the therapy can be used "as respiratory support in critically ill patients for a number of indications, including respiratory failure or support post-extubation."[3]

Here are four reasons why clinicians should rethink the use of HFNC in a broader population of patients moving forward.

1. Lower risk for complications

Endotracheal intubation has been common practice when treating respiratory distress, but it comes with a variety of potential risks, including airway damage and infection.[4,5,6]

On the other hand, oxygen therapy delivered via HFNC is non-invasive and has been shown to reduce the rate of intubation, mechanical ventilation and the escalation of respiratory support in various groups of patients.[7,8,9,10] It can also reduce the risk for reintubation among extubated patients.[11]

2. More comfortable and convenient for the patient

Endotracheal intubation has historically been the first line of support for respiratory failure, but patients often suffer distress and discomfort while the tube is in place. For example, in one study, the majorty of patients who were intubated and on mechanical ventilation reported feeling afraid because they could not communicate verbally,[12] whereas HFNC facilitates normal speech.

HFNC administered via nasal cannula is non-invasive compared to intubation, making it a more convenient and comfortable option. Furthermore, studies show that high-flow therapy administered via nasal cannula is typically more comfortable for patients compared with noninvasive ventilation (NIV) via face mask.[13]

3. Offers a less traumatic intervention

Immediately intubating a patient in respiratory distress is not

Dräger HI-Flow Star Nasal Cannula
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always necessary and can increase the risk for complications. One study found more than one third of intubations in patients transferred to burn centers were unnecessary, exposing patients to unwarranted complications.[14]

By starting oxygen therapy with a HFNC and monitoring the patient's respiratory status, clinicians may delay or avoid intubation.[15] If a patient's status is stabilized while on HFNC, clinicians can continue with this therapy, potentially decreasing complications, ICU days and cost to the hospital.[16]

4. Enables a dual-approach to treatment

One article noted that despite certain issues, "a growing body of evidence suggests that HFNC oxygen therapy is an innovative and effective modality for the early treatment of adults with respiratory failure associated with diverse underlying diseases."[17] It allows for clinicians to administer additional therapies in conjunction with oxygen to treat a variety of conditions.

For example, HFNC can be administered alongside nitric oxide therapy for patients suffering from pulmonary hypertension. In fact, researchers believe the addition of high flow oxygen may drastically decrease the inhaled nitric oxide (iNO2) requirement in the treatment of pulmonary hypertension.[18]

Conclusion

Out of the devastation of the COVID-19 pandemic has come many lessons learned and best practices to carry healthcare delivery forward. The benefits of oxygen therapy via HFNC over endotracheal intubation in cases where this non-invasive therapy is appropriate were observed on certain SARS-CoV-2 patients at the University of Chicago Medicine and have since been extended to other care areas. Perhaps expanded use of HFNC will continue in the years ahead, offering clinicians a less traumatic and less risky intervention for patients in respiratory distress.

While HFNC has proven successful in many patients, others will still require intubation and mechanical ventilation. Still others may fare better with NIV via face mask.

When an organization is considering the purchase of ventilators, it should also consider the modes of therapy delivered, as well as the vendor's ability to support those modes with high quality consumables. That way, clinicians can switch a patient between traditional ventilation mode to HFNC or non-invasive mask to meet changing needs all while still using the same machine. This approach also supports successful transition of patients down on oxygen therapy to wean them/move them out of the ICU.

Note

Not all products shown are available for sale in the U.S.

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MOC-9 Module, clinicians can now obtain simultaneous, dual oximetry pre- and post- ductal measurements, using one display, and increase efficiency of CCHD newborn screenings with Root. Furthermore, the Eve application on Root is automated and therefore simplifies and systematizes the screening process. Millions of newborn babies and their families throughout the world will be greatly benefited by this unique solution."

Clinical Strategy Expert Joins Respiratory Therapy Advisory Board

Gary L Hansen, Director of Scientific Affairs for RespirTech, a Philips Company, has joined the Editorial Advisory Board of Respiratory Therapy—bringing with him years of expertise in developing clinical strategies that have produced improvements in the RT industry. His responsibilities with RespirTech include the acquisition of scientific, medical, and technical knowledge of importance to the company, the synthesis of such knowledge into a form that is usable by internal and external stakeholders, and the dissemination of the synthesized information in a way benefits patients and enhances company growth. Specifics include setting clinical strategy, designing scientific studies, and authoring manuscripts. Hansen's certifications are impressive: PhD in Biomedical Engineering, University of Minnesota; MS in Software Engineering, University of St Thomas; and a BS in Astronomy and Philosophy, Haverford College. Hansen's Academic Appointments include Industrial Fellow. Institute for Engineering in Medicine, University of Minnesota, in 2015, where he explored and pursued collaborative research initiatives, and communicated industry needs to University of Minnesota faculty and faculty expertise to industry.

NDD Welcomes Michael Bencak as New CEO

NDD Medical Technologies (NDD), a global leader and innovator of diagnostic devices for the early detection of COPD and other chronic lung diseases, announced the appointment of Michael Bencak as Chief Executive Officer. Michael has two decades of experience in the medical device and biotechnology industry, including most recently at BEKA Scientific GmbH and Zinsser Analytic GmbH as Chief Executive Officer, where he repeatedly produced sustained revenue and Earnings Before Interest and Taxes (EBIT) growth in dynamic and evolving markets. Michael joins NDD at an exciting time, with the company exhibiting rapid growth due to the increasing demand for spirometry and DLCO devices. NDD was founded by Professor Karl Harnoncourt and Dr. Christian Buess, now Chief Technology Officer, after identifying an urgent need for advancements in pulmonary testing. With consistent growth throughout their 25-year history, NDD is the global leader in lung function testing and pulmonary function test devices, with innovative devices such as the EasyOne® product line providing much-needed point-of-care solutions. Committed to improving the lives of patients with the early detection and diagnosis of COPD and other chronic lung diseases, at a time of accelerating demand for additional lung testing due to long-Covid, NDD prides itself on the development of new and innovative solutions. Former CEO and now Chief Strategy Officer, Georg Harnoncourt, said "NDD has provided innovative lung function testing devices since 1996, with the mission of helping physicians around the world to rapidly identify and diagnose respiratory disease. We are excited to welcome Michael to the NDD family. His exemplary leadership track record, a wealth of medical technology experience and proven ability to drive results, makes him the right leader to

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The Role of Noninvasive Ventilation in Neuromuscular Disorders

Wolfram Windisch, Anita Simonds and Peter Wijkstra

Pulmonary comorbidities, including chronic obstructive pulmonary disease (COPD), asthma and congestive heart failure, are frequently found in adults with neuromuscular diseases (NMD), particularly those with rapidly progressive disease such as motor neurone disease or amyotrophic lateral sclerosis (ALS).[1] As a result, healthcare utilisation for pulmonary complications is substantial, and depends on the age of the patient, with a higher frequency in those aged over 70 years. In a population study, more than one-third of adults with neuromuscular disease had undergone pulmonary outpatient clinic visits with a mean 6 visits per patients, pulmonary function testing in about a third, sleep studies in 14% and 16% having intensive care unit (ICU) admissions. There were disparities according to income level, and only a minority received ventilatory support. In patients with ALS, 6% received home mechanical ventilation (HMV).[1] Blood gases and lung function parameters vary substantially between patients with differing neuromuscular disorders when started on HMV: patients with ALS are very likely to have HMV but are typically referred late in the disease, compared with Duchenne muscular dystrophy (DMD) patients who tend to receive HMV earlier in the disease course.[2]

When considering the benefits of artificial ventilation, it is important to remember that the respiratory system consists of two components: the lungs and respiratory pump. Pulmonary failure leads to hypoxaemic respiratory failure, whereas pump insufficiency and ventilatory failure lead to hypercapnic respiratory failure. Oxygen therapy is not indicated in the latter scenario; artificial ventilation is needed. The management of respiratory failure in NMD requires the use of artificial ventilation to assist the respiratory muscles in order to correct the alveolar hypoventilation and ameliorate gas exchange.

The benefits of artificial ventilation were first demonstrated in 1953 during a polio epidemic, when the use of 24 hour manual ventilation caused mortality to plummet from 92 to 25%.[3] Since then, a wide range of NMD have been found to benefit from artificial ventilation, primarily by noninvasive ventilation (NIV). National guidelines have algorithms recommending when patients should be referred and offered NIV. German guidelines recommend considering NIV when patients are symptomatic, there is evidence of respiratory muscle weakness or forced vital capacity (FVC) falls below 70% of the predicted value. The decision should be individually tailored but it is important to start early when patients start to become hypercapnic.[4] Improved survival with NIV has been demonstrated in patients with progressive NMD, and also in some subgroups of patients with COPD, suggesting that the effect is NIV is not limited

to the respiratory pump.[5] In hypercapnic patients with DMD, NIV has a substantial impact on long term survival.[6] Other neuromuscular conditions include where NIV may be used include spinal muscular atrophy (SMA), X-linked myotubular myopathy, congenital muscular dystrophy and mitochondrial disorders.

Deciding when to initiate NIV can present challenges in patients with rapidly progressing NMD. It can be difficult to predict how quickly a disease is going to progress in a newly diagnosed person with ALS. Patients can be broadly categorised as rapidly progressive or less rapidly progressive but the decision can be difficult on an individual basis. Younger age at diagnosis, delay between symptom onset and diagnosis, and FVC are useful prognostic factors for respiratory insufficiency in ALS.[7] A recent study showed that the decline in vital capacity was rapid at first but slowed after about 17 months.[8] The introduction of NIV in childhood is associated with an increase in survival in a range of progressive conditions,[9] and has a favourable long-term impact on nocturnal and diurnal gas exchange.[10]

Identifying biomarkers of disease progression would be useful to inform treatment decisions. A randomised controlled trial in patients with ALS found that NIV improved survival in the subgroup of patients with mild/moderate bulbar weakness on study entrance. In patients with severe bulbar impairment, NIV improved sleep- related symptoms, but did not confer a large survival advantage.[11] Sleep disordered breathing, particularly nocturnal hypoventilation (NH) is a complication of respiratory involvement in NMD that can evolve into symptomatic daytime hypercapnia if not treated with NIV.[12] Respiratory polygraphy is generally used to detect NH; oxycapnography may also be used. Paediatric patients with NMD can develop NH in the absence of clinical symptoms or other signs of nocturnal altered gas exchange. Monitoring of nocturnal hypoventilation should, therefore, be included among nocturnal respiratory assessments of these patients as an additional tool to determine when to initiate NIV.[13]

Cough is impaired in NMD and therefore cough assisting is an important part of the management of the condition. Inspiratory weakness leads to a reduction of inspiratory volume, bulbar weakness impairs the glottis closure and expiratory weakness reduces cough pressure. Maximum insufflation capacity (MIC)

and peak cough flow (PCF) should be measured at each clinic. The latter is most important in terms of deciding when to start treatment. Peak cough flow should be 360–840 L/min. In clinical practice, a PCF between 160 and 200 L/min is considered an effective cough.

Airway clearance techniques include cough augmentation (assisted inspiration/expiration) and sputum mobilisation.[14] Manually assisted coughing and mechanical insufflation/ exufflation (MI-E) are effective and safe methods for clearing airway secretion in patients with NMD.[15] Breath stacking or airstacking with a mask and one way valve can achieve significantly increased lung volumes in NMD patients.[16,17]

In weaker patients, MI-E is the most appropriate choice. It has been shown to increase PCF, reduce dyspnoea and reduce the duration of the session, which is important for the patient.[18] It has also been found to be beneficial in NMD patients with upper respiratory tract infections.[19] It is important that inspiratory and expiratory timing/ pressures are individualized. Patients with ALS are likely to benefit from lower pressures, triggered insufflation and longer insufflation time. Greater exsufflation pressures than insufflation pressures, together with a shorter insufflation time than exsufflation time, should be used. Subjects who produced daily secretions are more likely to use MI-E every day.[20]

The use of MI-E is not supported by a strong body of clinical trial evidence; a 2013 Cochrane review found that only 5 studies with a total of 105 participants were eligible for inclusion, and concluded that there was insufficient evidence for or against the use of MI-E in people with NMD.[21] But despite the lack of evidence, experts consider that it must be used in weak patients with NMD.

In summary, this summary has demonstrated that management of respiratory failure in patients with NMD requires the use of NIV and that the management of cough impairment in weak patients requires MI-E. As patients with some NMDs are living longer, long term consequences of these interventions will arise; Clinical experience shows older patients now experiencing new, and some potentially fatal, complications of NIV. Further research is needed on how best to address these.

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build on NDD's heritage and steer our future development at this pivotal time of expanding innovation." Commenting on his new appointment as CEO, Michael Bencak says "I am delighted to join NDD. The business has a fantastic team and I feel honored to be able to build on the great foundations and innovative culture fostered by Georg and Christian. I am committed to the core values of our company and look forward to working closely with our exceptional team to accelerate innovation at this critical phase. Though global healthcare has always focused on the problem of emerging infections, the last 18 months have demonstrated that companies like NDD, who strive to not only be proactive but also reactive, are crucial to help build a better, more patient-oriented world."

Life Supporting Ventilator with High-Flow Oxygen Therapy Gets Commercial Launch

Movair, a respiratory therapy company formerly known as International Biophysics Corporation, announced the US commercial launch of Luisa, an advanced ventilator intended for use in homes, institutions, hospitals or portable applications for both invasive and non-invasive ventilation. Luisa can be used through the FDA's Emergency Use Authorization* in response to the increasing need for safe and effective ventilators. Luisa is a portable and compact home ventilator now available in the US and one of the first with the added benefit of high-flow oxygen therapy. For patients with chronic and acute respiratory conditions that require long-term ventilation, prolonged compliance is critical. Luisa was designed to help patients embrace everyday experiences and active, mobile lifestyles. Weighing only eight pounds, Luisa includes a battery run time of up to 18 hours and offers patients eight adjustable comfort settings to deliver personalized, tailored therapy. Luisa also features a rotatable 10-inch display and flexible connectivity options so patients can integrate the ventilator into current lifestyle habits such as sleeping on a certain side of the bed. Additionally, Luisa can be programmed in multiple languages, ensuring a multitude of diverse patients, families and caregivers receive understandable alarm notifications. "Life supporting ventilation with high-flow therapy using the Luisa device proved to be a true asset during the most recent COVID-19 surge," said Rami Arfoosh, MD, FCCP, Pulmonary and Critical Care Specialist and Associate Professor of Medicine at Medical College of Georgia, AU/UGA Medical Partnership. "It provided a new option to meet the high-flow needs for some patients in their home environment. Those patients would have otherwise continued to occupy hospital beds because of the lack of equipment that meets their needs at home. Luisa also provides the unique feature of switching back and forth between high-flow nasal cannula (HFNC) and non-invasive ventilator (NIV) with different mode by the push of a button." Luisa provides respiratory support and utilizes all standard volume, pressure and mouthpiece ventilation modes with the added benefit of high-flow oxygen therapy that can support nocturnally ventilated patients during the day with a less intrusive nasal cannula. High-flow oxygen therapy delivers a blend of air and oxygen that meets or exceeds a patient's inspiratory flow demand to improve oxygenation and decrease the workload of breathing. "Increased respiratory patient illness, COVID-19 and product recalls have created a critical need for ventilators in the United States," said David Shockley, CEO of Movair. "We're addressing this demand with the launch of Luisa, a portable and compact home ventilator, designed and made in Germany that also
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Review Looks at the Use of Inhaled Nitric Oxide in Cardiovascular Surgery for Perioperative Pulmonary Hypertension in the US

Chris Campbell

Some treatments that are used for surgeries in the United States are also known as being off-label despite their wide acceptance by medical professionals.

A new review has been released that looks at the frequent use of inhaled nitric oxide (iNO) in certain surgeries, despite it being off-label in the US. What the review found is iNO has a high level of effectiveness in these settings. Published with the titled of Inhaled Nitric Oxide (iNO) in Cardiovascular Surgery for Perioperative Pulmonary Hypertension: A Review, the manuscript was supported by Vero Biotech LLC.

The review was put together by Jayne Prats (literature search, manuscript preparation), a consultant to Vero Biotech, David Stocker (manuscript review), who is Chief Operating Officer of Vero Biotech, and Charles Pollack (manuscript preparation), who is Vice President Medical Communications and Scientific Affairs, Vero Biotech. The review authors detail what they were aiming to achieve by looking at how iNO is used in the US.

"Observational data indicate that nitric oxide (NO) gas has been widely used in pediatric and adult cardiac surgery in the US for over a decade, whether administered by inhalation/ventilation or directly into the cardiopulmonary bypass circuit," the review says. "This perioperative use of iNO in cardiac surgery is consistent with labeled indications in other, ex-US jurisdictions, and has become standard practice in many large centers in the US. Such use, however, while approved in several regulatory jurisdictions worldwide, remains off-label in the US. In this review, the mechanism of action for NO and its clinical relevance to cardiac surgery is presented, including preoperative, intraoperative, and postoperative periods (collectively, 'perioperative')."

Part of the review includes observational data from US practice during the past decade, with data that consistently show that the use of NO in cardiac surgery is "common and has in fact become a practice standard at many institutions. Although the use of inhaled NO (iNO) in the US remains off-label, reviews by the European Medicines Agency (EMA), Australian, Japanese, and various Latin American health agencies have granted a label indication for inhaled NO based on these data, which were interpreted as supportive of patient safety and have important and consistent efficacy signals."

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Significant Pharmacological Advance

Nitric oxide for inhalation was approved by the FDA in the US in 1999, the review says, with the "single indication to improve oxygenation and reduce the need for ECMO in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure (HRF) associated with clinical or echocardiographic evidence of pulmonary hypertension, termed 'PPHN' for persistent pulmonary hypertension in the newborn, in the hospital setting. With NO widely available in many US hospitals, there have been notable increases in use outside the neonatal intensive care unit, particularly in the cardiac catheterization laboratory and in the perioperative management of patients undergoing major cardiothoracic surgery and orthotopic organ transplant surgery."

The review details just how clinically relevant iNO is in cardiac surgery. "Inhaled NO is a potent selective dilator of pulmonary vessels and therefore can directly reduce pulmonary vascular resistance (PVR)," the authors write. "Thus, iNO therapy as a selective pulmonary vasodilator in cardiac surgery, with the specific goal of lowering pulmonary pressure, represents a significant pharmacological advance in managing perioperative pulmonary hemodynamics and life-threatening right ventricular dysfunction (RVD) and failure in this setting. The mechanism of action of inhaled NO is well understood; after inhalation into the alveolus, NO produces smooth muscle relaxation by increasing intracellular levels of cyclic guanosine monophosphate (cGMP) within the pulmonary vascular smooth muscle.[1] This leads to the activation of cGMP-dependent kinases (cGKs), which in turn leads to the activation of myosin phosphate and a subsequent release of calcium from intracellular stores, thereby allowing smooth muscle cells to relax. As the NO further diffuses into the vessel lumen, it is bound to and inactivated by oxyhemoglobin. The bound hemoglobin is converted to methemoglobin and further reduced to nitrates and nitrites. Therefore, the vasodilatory effects of NO are localized to the pulmonary vasculature and are short lived, because the half-life of cGMP is less than 1 minute."[2]

The authors also detail the use of iNO in cardiac surgery. "Pulmonary hypertension and elevated PVR in all clinical settings are usually responsive to iNO.[3] The vasodilatory effects of NO are localized to the pulmonary vasculature and are short lived, because the half-life of cGMP is less than 1 minute.[2] This allows the near immediate cessation of the effects of NO when it is removed from the respiratory circuit. This moment-to-moment,

highly localized effect is potentially both safe and efficacious in the critical care management of the cardiac surgical patient. On the other hand, the use of intravenous vasodilators may improve RV function,[4] but the systemic hypotension associated with the use of these agents may further impair myocardial perfusion and ventricular function, especially in the perioperative environment. Most of our understanding of the use of iNO in cardiac surgery comes from consistent data derived from small observational or single center randomized trials. Nonetheless, perioperative iNO has been approved for use in both children and adults in multiple regulatory jurisdictions, while in the US, off-label use of iNO in this setting is often the most frequent use of iNO in hospitals with cardiac surgery capability. Therefore, perioperative iNO represents a 'practice standard' in cardiac surgery even though iNO use is off-label in this setting and cannot from the clinical trial literature be considered a 'gold standard.'"

Looking at the Data

The authors of the review looks at all available published clinical trial literature on the use of iNO in the perioperative management of patients undergoing cardiac surgery and experiencing PH or acute right ventricular decompensation. What they found was that the literature "reflects a concordance of clinically meaningful results indicating safety and efficacy. While the literature is neither particularly broad nor deep, with only a few well-designed, rigorously executed, adequately powered studies with consistent dosing and duration of treatment, and while there is an absence of a statistically significant mortality effect attributable to iNO, there are consistent findings."

The review then details what those consistent findings are. They include:

- reduction in pulmonary artery pressure and PVR among patients with acute PH in the perioperative environment;
- selective effect on pulmonary hemodynamics as evidence by the lack of systemic hypotension as an adverse event (AE) in these trials;
- similar efficacy in infants (10-20 ppm), children (10-20 ppm), and adults (2040 ppm);
- general trends towards improvement in important clinical and pharmacoeconomic outcomes such as time to weaning off cardiac bypass, RV function support, intubation time (and success of extubation), and length of ICU stay are seen with NO perioperatively;
- lower incidence of post-operative acute kidney injury (AKI) associated with cardiopulmonary bypass;
- pervasive safety, as indicated by a general absence of consistent or persistent adverse effects in this setting, including clinically significant methemoglobinemia;
- lack of a comparator found to be more effective or safer.

"There are also additional biologically plausible signals that perioperative iNO in patients undergoing cardiac surgery and experiencing PH or acute RV decompensation experience," the review states, including:

- lower incidence of intra- and post-operative myocardial injury;
- improvement in intra- and post-operative cardiac index;
- fewer perioperative pulmonary hypertension "crises".

"No large Phase 3 trial of iNO in the perioperative cardiac surgery space has been performed," says the review, citing two reasons:

- iNO is known to be effective in treating PH in all age groups, and therefore it would be unethical to perform a placebo-controlled trial.
- There is no universally accepted alternative gold standard therapy, and therefore, a comparator-controlled trial of iNO is not feasible. The current practice standard use of iNO means that enrollment in such a large trial would prove difficult to recruit.

The review also details other benefits of treatment of Perioperative Pulmonary Hypertension with iNO. "In cardiac applications, including transplants, PH can lead to right-sided heart failure and early death. Inhaled NO can reduce right ventricular stroke work while not reducing systemic blood pressure."

When it comes to using NO in pediatric cardiac surgery in the past 20 years, "there has been no regulatory action to expand the label for patients beyond term/near term neonates with PPHN. However, physicians at US children's hospitals have been increasingly using NO for off-label diagnoses. Available information suggests that this trend applies to most Children's Hospital Association (CHA)-member hospitals that participate in regularly sharing their performance data. The Children's Hospital Association surveyed its member hospitals in 2016 to determine trends in utilization of NO. The surveyed hospitals reported >15% off-label use, with 12 of the 22 hospitals reporting some use of NO finding an increase in NO use over 2013."[5]

Summary of Findings

The review finishes off with an emphatic statement about the use of iNO, which the authors call the "practice standard," and its effectiveness.

"Although the only US FDA-approved indication for iNO has remained for use in neonatal patients with persistent pulmonary hypertension, several other worldwide regulatory jurisdictions have approved iNO for perioperative use in adults and pediatric patients undergoing cardiac surgery. As outlined in this review, clinical trial and real-world data provide evidence that iNO is effective for reducing pulmonary hypertension in the perioperative setting. The use of iNO is widespread, and its use has become the practice standard for surgical teams."

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Nasal High-Flow Oxygen Therapy: Are All Solutions Designed Equally?

Chris Campbell

Background

Like other broad categories of medical devices, different brands of Nasal High Flow (NHF) therapy devices share similarities in operation, but also distinct differences in design characteristics. As a device category, NHF systems are designed to deliver relatively high flow rates of warmed, humidified gas via a nasal cannula to spontaneously breathing patients.

The growth rate in NHF therapy utilization over the 5-10 years preceding the COVID-19 pandemic exceeded that of Non-Invasive Ventilation (NIV) therapy. However, when early intubation and mechanical ventilation of COVID-19 patients proved to be less effective than anticipated, utilization of NHF therapy was catapulted to the forefront of care in many healthcare systems.

When healthcare systems scrambled to determine the most effective non-invasive therapy options for rapidly climbing numbers of COVID-19 patients, clinicians considered alternative therapy solutions, developed new protocols, and observed therapy results. While other respiratory support therapies showed unimpressive or inconsistent results, NHF oxygen (NHFO) therapy was proven to be a highly effective treatment option for many COVID-19 patients in many healthcare systems.[1]

As increasing numbers of healthcare systems experienced favorable results from NHFO therapy on COVID-19 patients, orders for NHF systems exploded. In addition, the favorable results on COVID-19 patients led many healthcare providers to transition NHF therapy to a frontline respiratory therapy for other respiratory distress conditions. [2]

This swift rise in NHF utilization has led to a significant increase in the number of companies introducing NHF systems, or new NHF options for existing invasive or Non-Invasive Ventilators. With more NHF offerings on the market from various companies, one thing is becoming clear, there are design differences between different NHF brands that clinicians should pause to understand before making purchase decisions for NHF systems.

Gaps in the Literature

The dramatic increase in the adoption of NHF therapy over the last two years has resulted in a situation where changes in clinical practice have outpaced academic publications regarding these changes. Where literature does exist, the focus is on general patient or care area considerations, general mechanisms of action, and non-inferiority comparisons to respiratory support therapies such as Conventional Oxygen Therapy (COT) and NIV.

Very little has been written about the fundamental differences in technology design between NHF systems, and even less written about how those differences may contribute to differences in outcomes, safety, comfort, or clinical workflow. This lack of published information concerning design differences between different models of NHF systems leaves potential purchasers of NHF systems with a notable void that will be mitigated in this article by highlighting a short list of design characteristics that may be materially different between various models of NHF systems.

Fundamental Differences in NHF Technology

At the highest level, there are two basic types of NHF solutions: Manufacturer designed self-contained systems which have controls to adjust humidification, flow, and air-oxygen ratios built into the device by the manufacturer, vs User-configured blender systems which providers create by configuring a humidification system and air-oxygen blender.

Manufacturer-Designed vs User-Configured NHF Systems

While user-configured NHF systems can function safely and effectively, self-contained NHF systems are designed by a manufacturer to make all system components work seamlessly together, which can offer several advantages, including:

- smart alarms to enhance patient safety
- expanded therapy setting options to better meet individual patient needs
- built-in flow generator to permit NHF therapy in locations without wall compressed air
- reduced noise levels – which can substantially impact patient comfort
- ability to send NHF therapy data to an electronic medical record
- interoperability with other hospital systems to enhance patient safety and workflow
- one-stop support services

In contrast, user-configured blender systems are assembled using individual components that were not designed specifically

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to work together as a system. While this approach may potentially seem cost-effective, it also includes hidden costs and inefficiencies, such as the need for daily or weekly calibration, the need to replace reusable components that are inadvertently thrown away, the challenge of managing a broad mix of humidifier and blender components, and reduced consistency and intuitive operation for clinicians.

As NHF becomes an important frontline therapy, it's anticipated that healthcare systems will increasingly require NHF devices to be manufacturer designed as a self-contained system like other medical devices used daily in alignmentwith ECRI's statement that "facilities that plan to offer HFNC therapy should seriously consider purchasing systems that are specifically designed for this clinical application."[3]

Built-in Flow Generator vs External Source of Compressed Air

The ability to deliver high flows is a fundamental requirement of a NHF system. However, how a given system generates its high flow rates is a potentially significant difference between NHF systems, including manufacturer designed self-contained systems.

NHF systems use one of two basic approaches to generate high flows: include a flow generator (also referred to as turbine or blower) within the NHF device or connect the NHF device to wall compressed air or some other external source of high-pressure compressed air.

- NHF systems which rely on external compressed air do not offer the NHF therapy location flexibility provided by systems with built-in flow generators. However, external sources of compressed air are typically capable of generating sufficient flow to deliver consistent flow during patient exhalation, which may influence therapy results for certain patients as described further below.
- NHF systems with built-in flow generators maximize the flexibility to provide NHF therapy where needed rather than where external sources of compressed air are available. The patient surges many hospitals experienced at various times due to the COVID-19 pandemic demonstrated how valuable this flexibility can be. However, it is also important to determine whether an NHF system with built-in flow generator is capable of providing consistent flow during patient exhalation, since this may have a material impact on patient results as discussed in more detail below.

Sufficient Flow Rates and Ability to Deliver Consistent Flow

NHF is a flow-based therapy and for many adult patients, including COVID-19 patients, high flow rates up to 60 L/min are recommended for patients in acute respiratory failure.[4] In addition, the ability to deliver consistent flow during the entire respiratory cycle — including the exhalation phase — can have a significant influence on therapy results for patients facing more challenging levels of respiratory distress or failure.

Some NHF devices are not designed with the ability to deliver flow rates up to 60 L/min, including some devices that have maximum flow rates of 40 L/min. A fundamental requirement of systems designed to deliver high flows is the ability to deliver flow rates which exceed the patient's inspiratory demand. Since it would not be uncommon for the inspiratory demand of patients in respiratory distress to be 45 L/min or higher, NHF systems should ideally be capable of delivering flow rates up to 60 L/min.[5]

One of the less recognized differences between NHF systems is the relative ability to maintain the user-selected flow rate during the exhalation phase of the patient's respiratory cycle. The reason the delivered flow rate may vary during the exhalation phase is simple: exhalation creates backpressure which could potentially reduce the delivered flow if the flow source is not able to adjust flow quickly enough. A system that is unable to maintain the desired flow during exhalation will be less effective in clearing out the nasopharyngeal dead space, which has been shown to play a significant role in flushing out CO2 while enhancing oxygen intake.[6]

As noted above, NHF systems which rely on external sources of high-pressure compressed air are typically capable of generating sufficient flow to deliver consistent flow during patient exhalation. However, NHF systems that use a built-in turbine to generate flow must be designed and able to instantly adjust flow delivery during the exhalation phase to overcome the backpressure caused by patient exhalation to maintain the user-selected flow during this critical phase of the respiratory cycle.

While assessing the flow rate range offered on a given NHF system is quick and easy, it is equally important to evaluate whether the device is capable of delivering the user-selected flow rate throughout the respiratory cycle. Bench tests can be set up to quantify the actual flows delivered by NHF systems during levels of backpressure created by exhalation. Furthermore, since this capability should impact how effectively CO2 is flushed out of the anatomical dead space, clinicians may be able to qualitatively assess this capability by performing brief comparative evaluations on patients with elevated CO2 and reduced SpO2 levels. If one of the devices being evaluated consistently provides reduced CO2 and improved SpO2, and possibly a reduced level of dyspnea when using the same flow rate and FiO2 settings as the other NHF device, it is a qualitative indication this NHF system is able to overcome exhalation backpressure to deliver the user-selected flow throughout the respiratory cycle.

Condensation

One of the fundamental attributes of a NHF system is the ability to warm and humidify the respiratory gas. Unfortunately, humidification creates the risk of condensation due to the fact that the humidified gas cools as it travels from the heated gas circuits to unheated cannulas in a patient environment that is cooler than the heated gas.

Condensation is so prevalent that some hospitals have instituted "empty" or "shake" protocols where clinicians schedule rounds to drain excess water from the circuit. This practice impacts clinical workflow while also creating undesirable risk. Emptying circuits of condensation requires interrupting therapy and "breaking" or opening the circuit, potentially increasing the risk of contamination entering the gas pathway or exiting the circuit into the patient environment. Alternatively, if water from condensation is left to build up in patient circuits, this can increase the risk of aspiration and secondary lung infections.

Most NHF manufacturers have attempted to mitigate condensation with sophisticated methods of heating the circuit. Some manufacturers have reduced the tubing diameter since

smaller tubing can be heated more easily than larger tubing.[7] However, since smaller tubing creates additional resistance to overcome when delivering flow to the patient, this approach requires a system with a powerful built-in flow generator or that uses an external source of compressed gas. Not all NHF systems are designed this way.

While these heated circuit improvements have helped reduce condensation from prior levels, most users believe that it remains a notable problem. After all, no matter how well the circuit is heated, a notable portion of the gas delivery circuit remains unheated… the nasal cannula. At least one NHF manufacturer believes this to be the case, and in response, they designed a one-piece circuit + cannula combination that heats the gas all the way from the device to the nose. This system design has not been tested, but logic suggests the approach is worth investigating.

Minimize Cross-Contamination Risk and Streamline Operational Efficiency

As one would expect, the significant harm associated with a COVID-19 infection led to a renewed focus on minimizing the risk of contamination, including between patients treated in the same environment and devices as well as between patients and caregivers. Although some differences of opinion remain regarding the best approaches to mitigate these risks with respiratory support procedures, most healthcare institutions and associated societies have determined that a combination of the following can safely address this risk:

- PPE designed for respiratory support therapy
- Consistent and effective use of bacterial-viral filters
- Single-Patient-Use (SPU) supplies, and
- Improved disinfection products and protocols

NHF therapy systems, like ventilators, are susceptible to cross contamination, so it is important to ensure any NHF system being considered is effectively designed to minimize the risk of cross contamination between patients, patients to care givers, and care givers to patients. With this important issue in mind, design considerations worth evaluating should include:

- Does the system in question include a SPU bacterial/viral filter between the flow generator and the patient? This is the preferred location for ventilators since it helps mitigate the risk of contaminants flowing from the patient to the device as well as from the device to the patient.
- Is respiratory gas delivered exclusively within a SPU gas delivery circuit which is replaced between patients, or do respiratory gases also flow through part of the device that cannot be replaced between patients? And if the device serves as a part of the respiratory gas delivery circuit, what disinfection process is required to ensure the device is safe for the next patient?
- Based upon the system design, how cumbersome and time consuming is the process to safely clean and disinfect the device between patients?

Conclusion

The COVID-19 pandemic created a myriad of respiratory therapy challenges that required healthcare institutions and clinicians to consider alternative therapy solutions. NHF therapy was proven to be a very effective treatment option for many COVID-19 patients, and as a result, NHF became a frontline therapy for COVID-19 as well as a variety of other respiratory distress conditions.

As NHF utilization has increased, the gap between what is being done in practice and clinical literature describing practice has increased. NHF can be delivered with systems of various types of designs and technologies, each with their own set of benefits and tradeoffs. Most existing publications treat NHF as a solution category and stop short of identifying potential tradeoffs between design characteristics of available solutions within the category. This article has endeavored to put a spotlight on a hand full of potential differences in design characteristics of widely available NHF systems that may contribute to differences in outcomes, safety, comfort, and clinical workflow.

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A Worldwide Review of Pre-Analytical Errors in Blood Gas Testing

J Conant, J Cervera

Introduction

It is well documented that the pre-analytical phase can contribute to up to 75% of errors in laboratory testing.[1] Many laboratories routinely track pre-analytical errors, as a part of sample validation and quality improvement initiatives. In point-of-care (POC) blood gas testing, these metrics are often not available or not discussed in the literature. POC and blood gas testing have challenges, not found in routine laboratory testing. POC operators may have varying levels of expertise with performing testing as they prioritize patient care, contributing to errors with impact on patient results.[2]

To help mitigate pre-analytical factors, the GEM® Premier™ 5000 system with Intelligent Quality Management 2 (iQM®2) (Werfen, Bedford, MA) offers detection of errors before, during and after sample measurement. This evaluation utilizes iQM2 data to offer new insights into prevalence of errors in blood gas testing detected based on transient error, micro-clots, and interferences in samples.

Methods

The GEM Premier 5000 system provides rapid analysis of heparinized whole blood samples at a POC setting or in a central laboratory. This system, together with its all-in-one multi-use GEM PAK cartridge, provides quantitative measurements of pH, pCO_2, pO_2, sodium, potassium, chloride, ionized calcium, glucose, lactate, hematocrit, total bilirubin and CO-Oximetry (tHb, O_2Hb, COHb, MetHb, HHb and sO_2^*) parameters. These measurements, along with a broad spectrum of derived parameters, aid in the diagnosis of a patient's acid/base status, electrolyte and metabolite balance and oxygen delivery capacity. iQM2 provides continuous monitoring of the analytical process before, during, and after sample measurement with real-time error detection, correction and documentation of all corrective actions, replacing the use of traditional quality control (QC).

iQM2, patented and exclusive to the GEM Premier 5000 system, detects, corrects and documents errors, due to pre-analytical factors, that could potentially affect results. This evaluation was focused on the errors detected by the following iQM2 checks:

- Pattern Recognition checks: applied to every patient sample to identify common sources of error (*e.g.*, micro-clots or fibrin strands on sensors, interference bybenzalkonium, thiopental, CO-Oximetry-specific interferences).
- IntraSpect™ checks: detects transient sample-specific errors through pattern recognition, using the patient sample as a control during the patient-sample measurement process. During this process, IntraSpect technology collects a series of sensor output readings. It then applies Pattern Recognition software to detect abnormal sensor behavior caused by a transient event with the potential to affect sensor performance (*e.g.*, micro-clots, micro-bubbles). IntraSpect is a novel form of quality assurance using the patient sample, essentially as its own control. Errors detected by IntraSpect are virtually impossible for the traditional ampoule-based QC methodology to detect.

In addition to Pattern Recognition and IntraSpect, iQM2 offers complete quality assurance with a continuous cycle of five checks, described below, but not evaluated in this study:

- Sensor/CO-Ox checks: perform 5 levels of process control solutions (PCSs) over 24 hours for real-time error detection.
- System checks: monitor the function of vital hardware components before each sample analysis (sensors, optics, pumps, electrical and mechanical controls).
- Stability checks: verifies stability of PCSs and cartridge integrity during GEM PAK use-life.

Data from more than one million samples, from 4,985 GEM PAKs used clinically in 2,765 GEM Premier 5000 systems, in 43 countries, were reviewed and analyzed. Data analysis focused on errors caused by pre-analytical factors, detected by iQM2.

Data was categorized by geographic area to identify potential differences in pre-analytical factors, by location.

Results

Pre-analytical sources of errors were detected, corrected and documented. Prevalence is indicated in Table 1.

Conclusion

Based on the global data analysis, pre-analytical errors in blood gas testing can impact approximately 1-2 in every 100 samples. Previous studies[2,3] demonstrated the impact of the pre-analytical and transient errors in blood gas testing and therefore, the ability to routinely detect, correct and document such errors offers a unique opportunity to ensure patient safety. Differences observed between geographical areas, especially for micro-

Werfen, Bedford, MA, USA. Presented at the 72nd American Association for Clinical Chemistry (AACC) Annual Scientific Meeting, December 13-17, 2020.

Table 1.

Pre-analytical category	Error detected by iQM2	Prevalence (%)				
		North America	South America	Europe	Asia	Oceania
Improper mixing/ anticoagulant	Micro-clots	0.69	0.70	0.84	0.53	1.01
Inadequate sample preparation and/or patient-specific treatment	Benzalkonium chloride	0.04	0.06	0.10	0.11	0.13
	Thiopental	0.00	0.03	0.02	0.02	0.03
	CO-Ox interferences	0.15	0.23	0.23	0.23	0.19
Transient errors	IntraSpect	0.53	0.94	0.89	0.69	0.98
	Total	1.41	1.96	2.08	1.58	2.34

clots and transient/sample-specific errors, indicate possible differences in pre-analytical factors that contribute to higher error detection rates.

* sO_2 = ratio between the concentration of oxyhemoglobin and oxyhemoglobin plus deoxyhemoglobin

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Pulmonary Function Testing and Reporting in the COVID-19 Era

Douglas C Johnson, MD

Abbreviations: 6MWT – 6 minute walk test; ARDS – acute respiratory distress syndrome; BMI – body mass index; CT – computerized tomography; DLCO – diffusing capacity of the lung for carbon monoxide; EMR – electronic medical record; FET – forced expired time; FEV1 = forced expired volume in 1 second; FVC = forced vital capacity; KCO = DLCO/VA; ICU = intensive care unit; SpO2 – oxygen saturation; PC20 – provocation concentration of methacholine leading to 20% fall in FEV1; PEF – peak expiratory flow; PIF – peak inspiratory flow; PFT – pulmonary function testing; sGaw – specific conductance; VA – alveolar volume (volume of tracer gas during DLCO maneuver);

SARS-CoV-2 was identified as the cause of COVID-19 in December 2019[1] and has led to a global pandemic leading to over 46 million reported cases, 3.2 million hospitalizations and 750 thousand deaths in the United States as of November 2021.[2] SARS-CoV-2 infection causes a wide range of disease, including lung damage and impaired lung function, which may progress to ARDS in over 20% of hospitalized patients.[3] We are learning more about the management and pulmonary abnormalities of patients with acute COVID-19 and of those who survive COVID-19.

The term "post-acute COVID-19 syndrome" has been proposed to define symptoms and abnormalities persisting beyond 12 weeks of the onset of acute COVID-19.[4] Many long-term complications of COVID-19 have been reported including general assessment, respiratory, psychiatric, neurologic, cardiovascular, renal, ear-nose-throat, endocrine, dermatological, and gastrointestinal with most patients having multiple and overlapping symptoms.[5]

Pulmonary symptoms including cough and dyspnea, and pulmonary function abnormalities are often present at hospital discharge and can persist for at least months. Abnormal DLCO and low lung volumes are more common than abnormal spirometry. Dyspnea can persist following improvement in pulmonary function.

At the time of hospital discharge from COVID-19, Mo et al[6] found spirometry was near normal with FEV1 93% predicted and FVC 95% of predicted, but there was lower TLC (87% predicted in mild, 79% predicted in severe cases), lower DLCO (85% predicted in mild, 65% of predicted in severe cases), with lower KCO (DLCO/VA) only in severe cases (99% predicted in mild, 83% predicted severe).

The prevalence of abnormal lung function among COVID-19 patients requiring ICU admission is much higher than those not requiring ICU admission. In non-critical COVID-19 patients studied 3 months following hospital discharge, 25% had abnormal pulmonary function, mainly reduced DLCO.[7] In COVID-19 patients requiring ICU admission studied 3 months following hospital discharge, symptoms of dyspnea (46.7%) and cough (34.4%) were common, with 82% having lung diffusing capacity below 80% and 70.2% with abnormal chest CT scans.[8]

In a study of hospitalized and non-hospitalized patients 4 months after COVID-19 diagnosis, most (68.6%) had symptoms including dyspnea (42.7%) and weakness (29.8%), and patients who developed pneumonia during COVID-19 compared to those without pneumonia had lower forced vital capacity, total lung capacity, SpO2 at rest and during 6MWT, and airway occlusion pressure 0.1s.[9]

A study[10] comparing mild/moderate to severe/critical patients 4 months after initial COVID-19 symptoms found that the severe/critical patients had worse radiologic abnormalities, lower % predicted FEV1, FVC, DLCO, TLC, higher FEV1/FVC, no difference in respiratory muscle forces, and lower 6MWT distance and 6MWT O2 nadir.

A study[11] comparing non-severe to severe COVID-19 patients 3 months after hospital discharge from COVID-19 found that the severe patients had more reduced DLCO (68% severe vs 42% non-severe <80% predicted) but not more reduced KCO (43% severe vs 38% non-severe <80% predicted).

While we are not aware of studies of airways reactivity among post-COVID-19 patients, we have had post-COVID-19 patients with normal spirometry and persistent cough and dyspnea having increased airways reactivity during methacholine challenge testing.

Cardiopulmonary exercise testing in post-acute COVID-19 syndrome patients[12] with persisting exercise limitation unexplained by conventional studies (e.g. normal PFTs and cardiac ECHO) nearly one year post COVID-19 found a peripheral rather than central cardiac limit to exercise, having a reduced peak exercise aerobic capacity associated with impaired oxygen extraction despite a preserved peak cardiac index,

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as well as having greater ventilatory inefficiency without an increase in dead space ventilation.

An international task force recommended follow-up of hospitalized COVID-19 patients with persisting respiratory symptoms 6-8 weeks following hospital discharge with measures of lung function.[13] Many non-hospitalized COVID-19 patients also have persisting symptoms of dyspnea and cough, so may be referred for pulmonary function testing to help evaluate lung function and assist with appropriate management. Given the vast numbers of post-acute COVID-19 syndrome patients often with persisting cough and dyspnea, many will be referred for pulmonary function testing.

Pulmonary function studies may include pre- and post-bronchodilator spirometry, lung volume, airway resistance and specific conductance, lung diffusing capacity of carbon monoxide, oximetry at rest and exercise, 6 minute walk test, respiratory muscle forces, arterial blood gas, methacholine challenge testing, and cardiopulmonary exercise testing.

Pulmonary function tests (PFTs) are important tools in the evaluation of the respiratory system. Interpretation of pulmonary function depends upon comparison of the patient's results to a normative sample to help distinguish between health and disease and to assess the severity of any impairment. Therefore it is important to have a PFT system which allows selection of appropriate reference equations, review of efforts by the interpreting physician, and reporting of results. These reference equations typically take into account sex, age, height, often race, and sometimes weight. Since predicted DLCO and KCO are also affected by hemoglobin, barometric pressure (or altitude), CO-Hb, Met-Hb, and lung volume, the PFT system should allow for these adjustments as well. Results for O2 saturation and arterial PO2 are influenced by altitude and inspired O2.

The Global Lung Initiative provides reference values for some spirometry values[14] for 4 ethnic groups, and for lung volumes[15] and DLCO for Caucasian subjects age 5-85[16] which account for age, sex, and height. There is a need for lung volume and DLCO prediction equations for Black and Asian, as using Caucasian equations leads to large discrepancies in predicted vital capacity from spirometry compared to lung volume or diffusing capacity maneuvers. We estimate Black and Asian lung volume and DLCO values as a fraction of Caucasian so the predicted results are more consistent with those for spirometry. Other reference equations are used for other spirometry values such as PEF. Equations for 6MWT distance[17] include weight and predict increased 6MWT for very obese subjects, so we substitute what the weight would be if BMI were 25 for those with BMI under 25 and if BMI were 35 for those over BMI of 35.

Spirometry is very helpful to assess whether there is airflow obstruction as can occur with asthma or COPD, decreased breath size as can occur with restrictive lung disease or moderate to severe obstruction, reduced peak flow relative to FEV1 with a plateau of expiratory flow as can occur with upper airway obstruction, or increased flows relative to vital capacity as can occur with interstitial lung disease. Emphysema typically has much lower flows on expiration relative to inspiration than does asthma. Improvement in spirometry to normal following bronchodilator is consistent with reactive airways, and significant improvement with normal DLCO is consistent with asthma, while significant obstruction with low DLCO suggests emphysema.

Lung volume is often elevated with emphysema, may be elevated with asthma, and lung volume is reduced with restrictive lung disease including interstitial lung disease and is often low in post-COVID-19 patients. Lung volumes may be overestimated by plethysmography when there is severe obstruction particularly if breathing frequency is not slow during the maneuver. Lung volumes may be underestimated by helium dilution or nitrogen washout when there is severe obstruction if there is insufficient time. The VA measured during single breath DLCO is the volume in which the tracer gas equilibrates minus the estimated anatomic dead space. For patients without significant obstruction the VA should match very close to the total lung capacity measured by plethysmography or helium dilution minus the estimated anatomic dead space.

Plethysmography often also measures airways resistance and specific conductance, which can be helpful to confirm or question airflow obstruction. Specific conductance (sGaw), which is measured near FRC, is typically low (<0.12) with airway obstruction, so a low sGaw in the setting of low FEV1/FVC confirms airway obstruction. Low sGaw can occur with normal FEV1/FVC when there are low flows at low lung volumes, so a low sGaw with low FEF75% is consistent with small airways obstruction. A normal or above normal sGaw in the setting of low flows and low PEFR raises concern for poor effort or respiratory muscle weakness rather than airway obstruction as the cause of the low flows. Similarly a normal sGaw in a patient with normal FEV1/FVC but very low inspiratory flows supports poor effort as the cause of the low inspiratory flows as opposed to extrathoracic upper airway obstruction, and vice versa.

The diffusing capacity of the lung for carbon monoxide (DLCO) is an important measure of the lung's ability to perform gas exchange. The single-breath DLCO is the standard method of measuring DLCO either using helium as the tracer gas collecting an expired sample after excluding the initial exhaled volume, or using methane as the tracer gas and a rapid gas analyzer of exhaled gas. DLCO is a sensitive measure for many types of lung disease, including those affecting the pulmonary vasculature (e.g. pulmonary embolism), alveoli (e.g. emphysema), and alveolar membrane (e.g. interstitial lung disease or low lung volume from chest wall abnormality) and is often low in post-COVID-19 patients. DLCO depends upon many factors—including getting CO to the alveoli, transfer across the alveolar membrane and combining with hemoglobin in blood.

DLCO, like other pulmonary function parameters, is influenced by age, height, sex, and race. Unlike spirometry or lung volume, several other factors influence DLCO including hematocrit, barometric pressure (or altitude), COHb, MetHb, and the lung volume at which DLCO is measured. Since DLCO depends upon alveolar surface area, changes in lung volume with otherwise normal lung tissue also affect DLCO. The terms DACO and KACO refer to DLCO and KCO predicted values that have been adjusted for lung volume.[18] Just as adjusting predicted DLCO and KCO for hemoglobin in an anemic patient yields a better indication of the lung's ability of gas exchange, adjusting DLCO and KCO for lung volume in a patient with low lung volume yields a better indication of the lung's ability of gas exchange.

DLCO and KCO change with lung volume in a manner expected from having DLCO depend on the surface area for gas exchange with the capillary blood component unchanged.[19] The following equations,[19] included in the 2005 ATS/ERS DLCO standards,[20] describe the effect of lung volume on predicted DLCO and KCO (Figure 1) as determined in normal subjects which match theoretic values which has DLCO changing as expected from the membrane component of DLCO depending on surface area. DLCO is about 80% and KCO about 160% at a VA of 50%.

DLCO[predicted for lung volume]=DACO (predicted) = DLCO[predicted]×(0.58+0.42×(measured VA/predicted VA))

KCO[predicted for lung volume]=KACO (predicted) = KCO[predicted]×(0.42+0.58/(measured VA/predicted VA))

Since predicted KCO = predicted DLCO / predicted VA, %predicted KACO equals % predicted DACO.

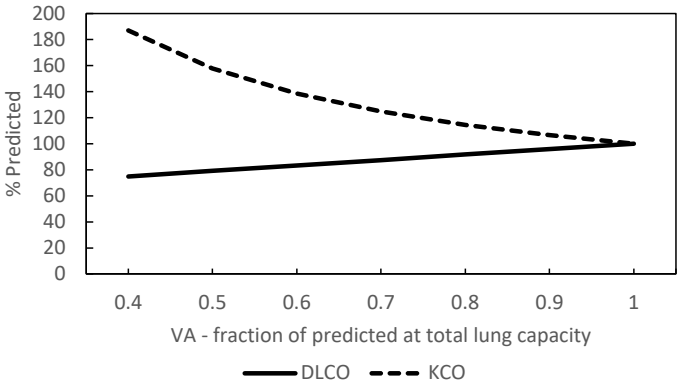

Figure 1. %Predicted DLCO and KCO versus VA (fraction of VA predicted at total lung capacity)

A low diffusing capacity was the most common PFT abnormality found among post-acute COVID-19 patients. It is no surprise that the studies of post COVID-19 patients found that while DLCO was below 80% predicted in most subjects, KCO (DLCO/VA) was usually normal. Many COVID -19 patients have reduced lung volume, so the predicted KCO at the low lung volume would be expected to be much above 100% of normal if diffusion was normal. Their %predicted DACO and KACO would be expected to be low. Mo et al[6] incorrectly refer to DLCO/VA as "The DLCO corrected for alveolar volume." Instead DLCO/VA (or KCO) is simply the DLCO divided by the VA (the lung volume in which the CO distributes during the test).

A low DACO (% predicted) indicates the lung's diffusion capacity when adjusted for lung volume is low. This can occur with interstitial lung disease (ILD), emphysema, or pulmonary vascular disease. VA is typically low with ILD, and normal with emphysema (VA often underestimates TLC in emphysema due to the tracer gas not fully equilibrating), asthma, and pulmonary vascular disease. This results in KCO about equal to DLCO in emphysema, asthma, and pulmonary vascular disease. Patients with ILD typically have low lung volumes and thus KCO higher than DLCO and KCO may be low, normal, or elevated in ILD. Patients with emphysema would be expected to have obstruction on spirometry, elevated lung volumes, and low DACO. Patients with asthma having obstruction on spirometry would be expected to have normal DLCO and DACO. Patient with normal spirometry, normal lung volumes, and very low DLCO could have pulmonary vascular disease, or if heavy smoking history a combination of emphysema and interstitial lung disease.

A normal DACO means the lung's diffusing capacity when adjusted for lung volume is normal. This can occur with normal lungs, and in patients with low VA not due to intrinsic lung disease such as neuromuscular weakness, chest wall deformity, or not inspiring to total lung capacity during DLCO testing. Subjects with low lung volume but normal intrinsic lungs will have low DLCO, elevated KCO and normal DACO. It is worth noting some patients with neuromuscular disease or chest wall deformity may develop atelectasis which could reduce DACO.

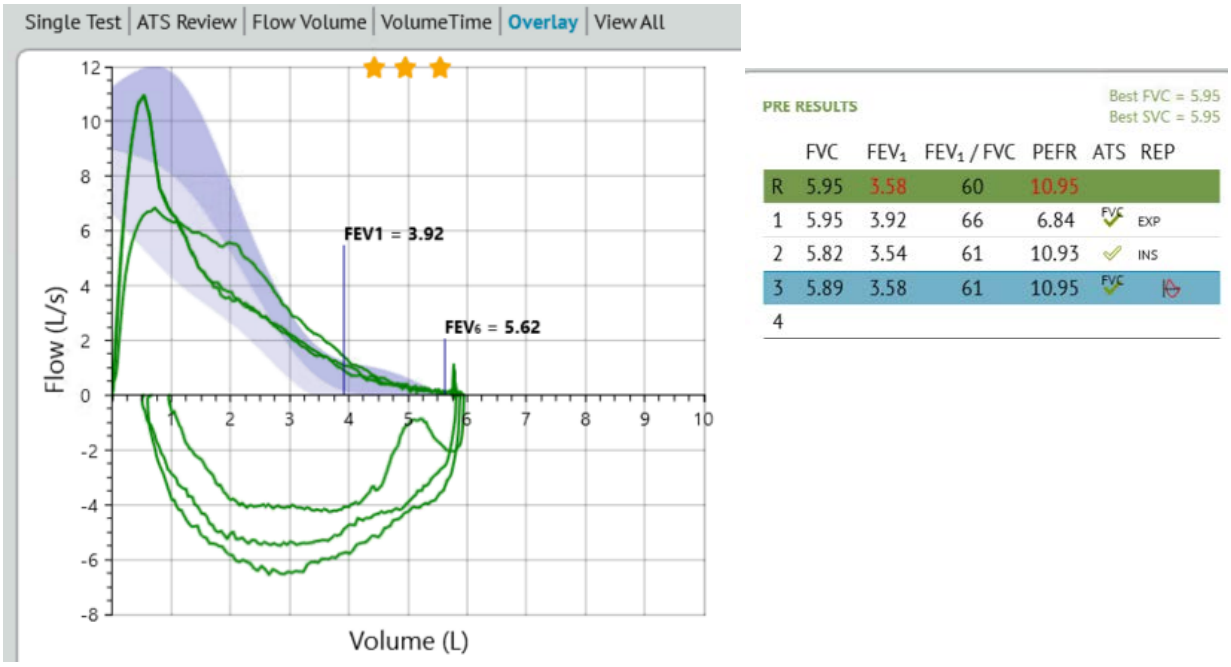

Figure 2. Higher FEV1 (effort 1) during submaximal effort when the PEFR was lower than efforts 2 and 3. The FVC from effort 1 and FEV1 and PEFR from effort 3 were selected to be reported. Screen example from ComPAS2 - Morgan Scientific, Inc.

Spirometry — Pre Bronchodilator

		Predicted Range Mean	95%	Actual	% Pred
FEV_1	L	2.90	2.12	**1.83**	63
FVC	L	3.76	2.81	**2.09**	56
FEV_1 / FVC	%	77	64	**88**	114
FEF_{25-75} [ISO]	L/s	2.32	1.05	**2.20**	95
PEFR	L/s	7.74	5.67	**4.86**	63
FET	s	13.81	7.62	**6.90**	50
MVV	L/min	118.5	61.7	—	—
FEV_6	L	3.65	2.85	**2.09**	57

Figure 3. PFT report 2 months post COVID-19 (3/15/2021). Report from ComPAS2 - Morgan Scientific, Inc.

Methacholine challenge testing is often used to assess for increased airways reactivity in patients with symptoms suggesting asthma, but with normal spirometry. The likelihood of asthma increases the lower the PC20, with most asthmatics having PC20 below 8 mg/ml and most normal subjects a PC20 above 16 mg/ml.

Clinical interpretation of pulmonary function testing has been reviewed[21] and commented on.[18] In general, a value below the 5% lower limit of normal is considered abnormal. For several values including FEV1, FVC, TLC, and DLCO the LLN for ages 20-50 is near 80% of predicted, but at other ages and for other parameters the LLN may be much different than 80%. The PFT system should report predicted, LLN (and for some parameters ULN), measured, and %predicted values. With some recommendations for reporting z-values, that should be an option, though I do not find z-values helpful so do not include them.

It is important to assess the validity and reproducibility of testing, so the interpreting physician should be able to review all flow-volume loops and efforts and be able to select a different loop or parameter if there are problems with the computer selected result. For example, the FEV1 may be significantly higher on a submaximal effort having a reduced peak flow (Figure 2), so the FEV1 should be selected from the loop with higher peak flow and lower FEV1.

Assessing reproducibility is also important to evaluate bronchodilator response. If efforts are poorly reproducible a 12% improvement in FEV1 may not be significant, while an 8% improvement in FEV1 with larger improvement in FEF25-75% could be considered probably significant if pre- and post-bronchodilator efforts were very reproducible. FEF25-75%-ISO refers to the flow from the same portion of the expiratory volume during post-bronchodilator testing as was used during pre-bronchodilator testing, so should better reflect bronchodilator response than FEF25-75%.

Reporting of spirometry should include predicted, measured, and % predicted standard parameters including FEV1, FVC, FEV1/FVC, PEF, FEF25-75% and may include others such as FET, PIF, FEF75%, PEF/FVC, with post-bronchodilator results including measured and % change. Graphs including the best pre-and post- bronchodilator loops and volume time curves should be included.

Reporting of lung volumes should include the method and predicted, measured, and %predicted TLC, FRC, RV, RV/TLC, and may include other parameters as ERV and IC. For

Spirometry — Pre Bronchodilator — Post Bronchodilator

		Predicted Range Mean	95%	Actual	% Pred	Post	% Pred	% Chg
FEV_1	L	2.89	2.11	**2.34**	81	**2.40**	83	3
FVC	L	3.76	2.81	**2.49**	66	**2.64**	70	6
FEV_1 / FVC	%	77	64	**94**	122	**91**	118	-3
FEF_{25-75} [ISO]	L/s	2.32	1.04	**4.18**	180	**3.77**	163	-10
PEFR	L/s	7.73	5.66	**6.38**	83	**5.80**	75	-9
FET	s	13.80	7.61	**3.57**	26	**3.09**	22	-13
MVV	L/min	118.3	61.5	**115.6**	98	—	—	-
FEV_6	L	3.65	2.84	**2.78**	76	**2.75**	75	-1

Plethysmography

		Predicted Range Mean	95%	Actual	% Pred
TLC	L	6.25	4.97	**4.69**	75
VC	L	3.76	2.81	**2.49**	66
RV	L	2.15	1.30	**2.20**	102
RV/TLC	%	34	23	**47**	138
FRC	L	3.23	2.24	**3.51**	109
ERV	L	1.03	0.34	**1.31**	127
Raw	$cmH_2O/L/s$	1.70	0.60	**0.65**	38
sGaw	$L/s/cmH_2O/L$	0.26	0.11	**0.45**	173

Diffusing Capacity

		Predicted Range Mean	95%	Actual	% Pred	Hb Date: 5/17/2021
DLCO	mL/min/mmHg	21.72	16.05	**9.77**	45	Predicted adjusted for Hb of 12.5
DLCO	mL/min/mmHg	23.31	17.22	**9.77**	42	Predicted not adjusted for Hb
VA [BTPS]	L	6.10	4.82	**3.46**	57	
KCO	mL/min/mmHg/L	3.82	2.82	**2.82**	74	Predicted adjusted for Hb
VI [BTPS]	L	3.76	2.81	**2.59**	69	104% of VC
DACO	mL/min/mmHg	19.07	14.09	**9.77**	51	Adjusted for lung volume and Hb

DLCO and KCO 51% predicted adjusted for lung volume, Hb of 12.5 and barometric pressure

Measured values adjusted for barometric pressure.

Figure 4. PFT report 4 months post COVID-19 (5/27/2021). Report from ComPAS2 - Morgan Scientific, Inc.

Spirometry — Pre Bronchodilator

		Predicted Range Mean	95%	Actual	% Pred
FEV_1	L	2.88	2.09	**2.94**	102
FVC	L	3.74	2.79	**3.59**	96
FEV_1 / FVC	%	77	64	**82**	106
FEF_{25-75} [ISO]	L/s	2.30	1.03	**3.20**	139
PEFR	L/s	7.68	5.61	**7.71**	100
FET	s	13.79	7.60	**12.31**	89
MVV	L/min	117.7	60.9	**124.0**	105
FEV_6	L	3.63	2.82	**3.49**	96

Plethysmography

		Predicted Range Mean	95%	Actual	% Pred
TLC	L	6.25	4.96	**4.82**	77
VC	L	3.74	2.79	**3.62**	97
RV	L	2.17	1.30	**1.20**	55
RV/TLC	%	34	23	**25**	74
FRC	L	3.24	2.25	**2.82**	87
ERV	L	1.02	0.34	**1.62**	159
Raw	$cmH_2O/L/s$	1.70	0.60	**1.55**	91
sGaw	$L/s/cmH_2O/L$	0.26	0.11	**0.20**	77

Diffusing Capacity

		Predicted Range Mean	95%	Actual	% Pred	
DLCO	mL/min/mmHg	24.16	17.83	**14.20**	59	Predicted adjusted for Hb of 16.2
DLCO	mL/min/mmHg	23.24	17.15	**14.20**	61	Predicted not adjusted for Hb
VA [BTPS]	L	6.10	4.81	**4.34**	71	
KCO	mL/min/mmHg/L	3.81	2.81	**3.27**	86	Predicted adjusted for Hb
VI [BTPS]	L	3.74	2.79	**3.34**	89	92% of VC
DACO	mL/min/mmHg	20.42	15.07	**14.20**	70	Adjusted for lung volume and Hb

DLCO and KCO 70% predicted adjusted for lung volume, Hb of 16.2 and barometric pressure

Measured values adjusted for barometric pressure.

Figure 5. PFT report 10 months post COVID-19 (11/8/21). Report from ComPAS2 - Morgan Scientific, Inc.

plethysmography if airway resistance and specific conductance were measured, those should be reported as well.

Reporting of DLCO should include predicted, measured, and %predicted values for DLCO, VA, KCO, VI (and VI as % of FVC), and DACO. If Hb, CO-Hb, and/or Met-Hb are available, the %predicted values for DLCO, KCO and DACO should be adjusted for those with a statement of the Hb, CO-Hb, and Met-Hb values and date of the Hb.

We have found that there is often further improvement in lung function after 3 months following COVID-19. PFTs performed 2, 4, and 10 months following hospitalization 1/18-1/31/2021 for COVID-19 are shown in figures 3, 4, and 5. Note some improvement in spirometry at 4 months to normal spirometry at 10 months, restriction at 4 and 10 months, and improvement in DACO from 51% to 70% at 4 to 10 months with normal unadjusted KCO but low DLCO and DACO at 10 months. Chest CT scans from the same patient at hospitalization (Figure 6) and at 7 months post COVID-19 (Figure 7) are also shown.

Reporting of MIP and MEP should include predicted measured, and %predicted values, along with prior test results and change. Ideally the interpreting physician should be able to review the wave forms of the pressures during each test to confirm they were sustained for a second.

Reporting of ABG values should include predicted values, measured values (pH, PCO2, pO2, FIO2 if on Venturi or 100% FIO2), estimated values (HCO3, O2 sat, FIO2 if on nasal O2,

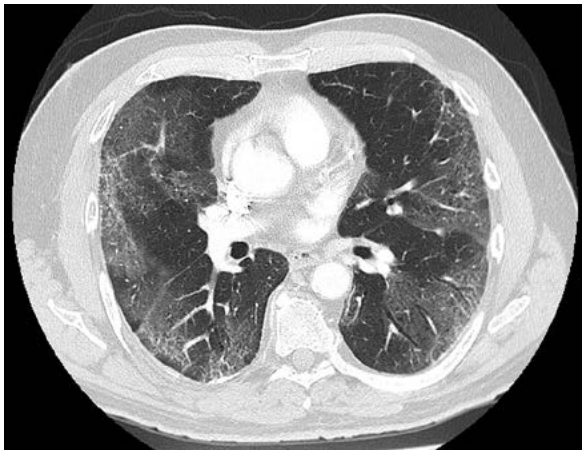

Figure 6. Chest CT at time of presentation (COVID-19 1/18/2021, CT 1/22/2021)

alveolar O2, A-a O2 gradient, shunt (if on 100% FIO2), with an explanation of how predicted values and estimated values were determined (e.g. whether adjusted for barometric pressure, FIO2, PCO2) such as figure 8.

Reporting of 6MWT should include whether on supplemental O2, resting and peak Borg dyspnea (and fatigue), O2 saturations, heart rate, and if measured blood pressure during and following the test, predicted, LLN, measured, and %predicted 6MWT distance along with prior 6MWT distance and change such as Figure 9.

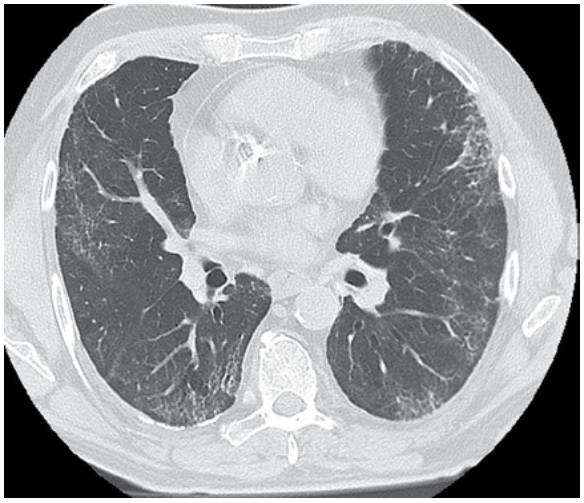

Figure 7. Chest CT 7 months later (COVID-19 1/18/2021, CT 8/16/2021)

Reporting of methacholine challenge testing should include predicted, measured, and %predicted values for spirometry parameters including FEV1, FVC, FEV1/FVC, PEFR, FEF25-75%, at baseline, after each methacholine dose, and post bronchodilator, along with a semilog graph of FEV1 (% of baseline) at baseline, after each methacholine dose, and post-bronchodilator, and the PC20 – the estimated concentration of methacholine at which there would be a 20% fall in FEV1, or whether the PC20 is below a value or greater than another value. Alternatively PD20 can be used.

All of the above PFT reporting should include comparisons to prior test results either in the report itself or in the interpretation. Some PFT systems allow tabular and graphic reports comparing current to prior tests. While reports comparing measured values are usually sufficient, for pediatric subjects who have large changed in predicted values with age, comparisons of %predicted values is very helpful. Having a robust computer impression which includes comparison to prior studies can facilitate physician interpretation.

Coordination of PFT systems with electronic medical records (EMR) is essential for PFT results to be readily accessible. This may include having a preliminary report going to the EMR as a pdf as soon as the study is completed, a final report going to the EMR as soon as the study is interpreted by the physician, and numeric values for some PFT parameters (e.g. FEV1, FVC, FEV1/FVC, TLC, DLCO and their %predicted) going to the EMR similar to laboratory results. We have used the Morgan Scientific ComPAS and ComPAS2 system which provides all the capabilities above including customized prediction equations, reporting, computer impressions, cardiopulmonary exercise testing, and integration with the EMR.

In summary, COVID-19 has affected millions in the United States, with many having symptoms persisting for many months following COVID-19 diagnosis that suggest abnormal lung function. Pulmonary function testing will play a key role in assessing lung function impairment in these post-COVID-19 patients. PFT systems which provide good test performance, reporting, interpretation, and are integrated with electronic medical records will facilitate those evaluations.

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ABG	FIO2	pH	PaCO2	PaO2	HCO3-	O2 Sat	AaDO2	Shunt
Normal room air values for age		7.36 to 7.44	36 to 44	65 to 89	22 to 26	93 to 97	13 to 37	
I-STAT ranges		7.36 to 7.44	36 to 46	80 to 96	22 to 29	96 to 100		
e - estimated			mmHg	mmHg	mEq/L	%	mmHg	%
Room Air	0.21	7.38	48.0	55.0	28.4	87 e	37 e	
2 L/min O2	0.26 e	7.34	54.0	75.0	29.1	94 e	48 e	
1.00 FIO2	1.00	7.32	58.0	500.0	29.9	100 e	155 e	8.5 e

ABG on room air shows hypoxemia with increased AaO2 gradient. There is hypercapnia with respiratory acidosis and a compensatory metabolic alkalosis.
ABG on 2 L/min O2 shows adequate PO2 on supplemental O2. There is significant hypercapnia with respiratory acidosis and a compensatory metabolic alkalosis.
ABG on 1.00 FIO2 shows good PO2 on supplemental O2. There is significant hypercapnia with respiratory acidosis and a compensatory metabolic alkalosis. The estimated shunt is 8.5%.

Figure 8. ABG report of simulated results with computer impression from ComPAS2 - Morgan Scientific, Inc.

Six Minute Walk Study

		Resting	1 min	2 min	3 min	4 min	5 min	6 min	Max	Recovery Min 1	Recovery Min 2	Recovery Min 3
SpO2	(%)	96.0	96.0	94.0	92.0	93.0	91.0	91.0	91.0			
HR	(bpm)	69	102	103	103	112	112	118	118			
BP	(mmHg)	120 / 80							150 / 80			
Dyspnea	(1 - 10)	1	----	----	----	----	----	----	3			
Fatigue	(1 - 10)	0							0			

Actual 6MW distance: **372** meters
Predicted distance: LLN: **312** **465** meters
Percent of predicted: **80** %

Supplemental oxygen during the test:
Previous Test:
Last Test Date: **10/23/2018** Last Test Distance: **471** meters

Figure 9. Example of a Six Minute Walk Study report from ComPAS2 - Morgan Scientific, Inc.

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Comparison of Airway Pressures and Expired Gas Washout for Nasal High Flow Versus CPAP in Child Airway Replicas

Kelvin Duong[1], Michelle Noga[2], Joanna E MacLean[3,4], Warren H Finlay[1] and Andrew R Martin[1,5]

Abstract

Background: For children and adults, the standard treatment for obstructive sleep apnea is the delivery of continuous positive airway pressure (CPAP). Though effective, CPAP masks can be uncomfortable to patients, contributing to adherence concerns. Recently, nasal high flow (NHF) therapy has been investigated as an alternative, especially in CPAP-intolerant children. The present study aimed to compare and contrast the positive airway pressures and expired gas washout generated by NHF versus CPAP in child nasal airway replicas.

Methods: NHF therapy was investigated at a flow rate of 20 L/min and compared to CPAP at 5 cmH_2O and 10 cmH_2O for 10 nasal airway replicas, built from computed tomography scans of childxqren aged 4-8 years. NHF was delivered with three different high flow nasal cannula models provided by the same manufacturer, and CPAP was delivered with a sealed nasal mask. Tidal breathing through each replica was imposed using a lung simulator, and airway pressure at the trachea was recorded over time. For expired gas washout measurements, carbon dioxide was injected at the lung simulator, and end-tidal carbon dioxide ($EtCO_2$) was measured at the trachea. Changes in $EtCO_2$ compared to baseline values (no intervention) were assessed.

Results: NHF therapy generated an average positive end-expiratory pressure (PEEP) of 5.17 ± 2.09 cmH_2O (mean ±SD, n = 10), similar to PEEP of 4.95 ± 0.03 cmH_2O generated by nominally 5 cmH_2O CPAP. Variation in tracheal pressure was higher between airway replicas for NHF compared to CPAP. $EtCO_2$ decreased from baseline during administration of NHF, whereas it increased during CPAP. No statistical difference in tracheal pressure nor $EtCO_2$ was found between the three high flow nasal cannulas.

Conclusion: In child airway replicas, NHF at 20 L/min generated average PEEP similar to CPAP at 5 cm H_2O. Variation in tracheal pressure was higher between airway replicas for NHF than for CPAP. The delivery of NHF yielded expired gas washout, whereas CPAP impeded expired gas washout due to the increased dead space of the sealed mask.

Keywords: Obstructive sleep apnea, Continuous positive airway pressure, Nasal high flow, Nasal cannula, Adherence, Tracheal pressure, End-tidal carbon dioxide

Background

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder in which an individual's upper airway is obstructed, causing partial to complete interruptions in their breathing. OSA affects both adults and children, but the consequences of the disorder may differ between the two groups. The negative impacts of OSA on cognitive, learning, and behavioural functions are more serious in children than in adults.[1-3] Other complications in children include cardiovascular complications and impacts on growth.[1,2,4,5] OSA is estimated to affect between 1 and 10% of children.[1,6-8]

The delivery of continuous positive airway pressure (CPAP) is an effective treatment for OSA in children.[9,10] CPAP restores breathing and sleep by acting as a pneumatic stent to prevent the collapse of the upper airways. Typically, a nasal/facial mask, preferably selected to conform as best as possible to the individual's facial geometry, is used to administer CPAP.[11] Though effective, adherence to the therapy is poor due to discomfort.[12,13] Multiple factors contribute to discomfort, such as mask leak, skin irritation, and/or pressure sores.[14,15] With the goal of improving adherence to CPAP therapy, several groups have investigated improvements to the comfort of the mask interface.[16-19] However, other groups have explored alternative forms of non-invasive respiratory support, including administration of nasal high flow (NHF) therapy.[20,21]

The most obvious difference in the administration of CPAP versus NHF is in the interface used. For CPAP, breathing gas is typically delivered to the patient through a tightly-fitted nasal or facial mask. Air, or an air/oxygen mixture, is delivered from a CPAP machine to the mask through a supply tube with an expiratory port (Figure 1). In contrast, during NHF therapy, air, or an air/oxygen mixture, is delivered through an open interface: a high flow nasal cannula. Unlike CPAP, no expiratory port is included in the supply tube, as exhaled gases are vented to the room through the open space around the nasal cannula prongs (Figure 2). For CPAP, the expiratory port acts both as an outlet for expired air, as well as a means through which the

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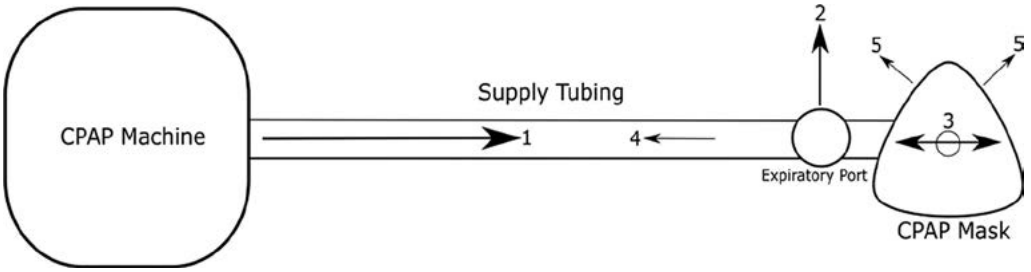

Fig. 1 Schematic of CPAP therapy with arrows indicating the flow direction of air. (Arrow 1) Flow of gas (air or air/oxygen mixture) provided by the CPAP machine. (Arrow 2) Flow of gas that exits the expiratory port on the supply tube. (Arrow 3) Cyclic flow of gas from the patient during inspiration and expiration. (Arrow 4) Backflow of air that may occur during expiration at high flow rate. (Arrow 5) Flow of air out of the mask when leaks exist between the mask cushion and face. *CPAP* continuous positive airway pressure

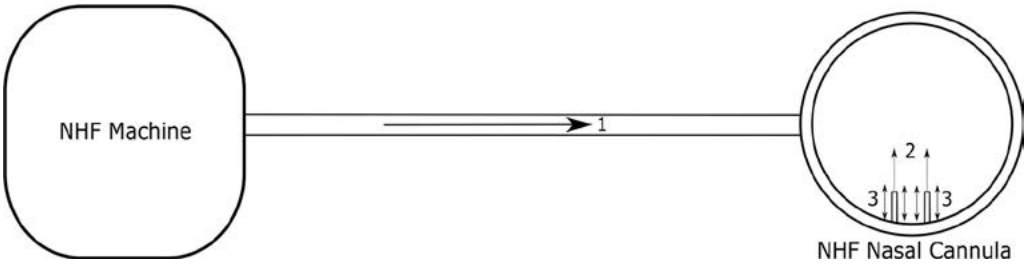

Fig. 2 Schematic of nasal high flow therapy with arrows indicating the flow direction of delivered gas (air or air/oxygen mixture). (Arrow 1) Flow of gas provided by the NHF machine (constant). (Arrow 2) Flow of gas that exits the nasal cannula prongs into the patient's nostrils. (Arrow 3) Cyclic flow of gas entrained by the patient during inspiration, or expelled during expiration, occurring around the nasal cannula prongs. *NHF* nasal high flow

CPAP machine generates pressure in the supply tube and mask. During breathing, the CPAP machine monitors pressure and continuously adjusts the flow rate of gas it delivers, in order to maintain a constant pressure in the supply tubing and mask. In contrast, during NHF therapy, gas is supplied at a constant flow rate, which does not adjust according to patient breathing. Pressure is not monitored during NHF therapy.

The delivery of NHF for OSA in children has been investigated as an alternative to mask-based CPAP.[20-22] NHF therapy generates positive airway pressure through the delivery of humidified air or air/oxygen mixtures at high flow rates through nasal cannulas. In studies by Hawkins et al.[22] and Amaddeo et al.,[21] both groups assessed NHF therapy in children who were intolerant to CPAP therapy. NHF therapy was shown to have good compliance in children and was able to reduce respiratory events.[21,22] The open interface of the nasal cannula may be more comfortable and tolerable than CPAP masks for overnight use.[20-22] Furthermore, in children, CPAP has been associated with hindered development of the face due to use of tight-fitting masks.[23] The use of NHF may avoid this issue. In addition to positive airway pressure, NHF therapy is known to provide washout of the nasopharyngeal dead space.[24] Washout may improve gas exchange, potentially contributing to correction of hypopneas and apneas in children with OSA.[21,22] These benefits make NHF therapy a promising alternative for CPAP-intolerant children.

In the present work, upper airway pressures and carbon dioxide washout were compared between NHF and CPAP therapy in vitro using child airway replicas coupled to a lung simulator.

Methods

In this in vitro study, the delivery of NHF through nasal cannula was compared with the delivery of CPAP through a nasal mask. The study was conducted using the upper airway replicas of 10 child subjects, with two main comparative measurements: tracheal pressures and end tidal carbon dioxide concentration ($EtCO_2$). Tracheal pressures were separated into four parameters: positive end-expiratory pressure (PEEP), peak expiratory pressure (PEP), minimum inspiratory pressure (MIP), and average inspiratory pressure (AIP).

Child airway replicas

The 10 upper airway replicas, which include the nose-throat airway and terminate at the trachea, were previously fabricated in our research group based on computed tomography (CT) scan data of 10 child subjects, between the ages of 4 and 8 years, as reported by Paxman et al.[25] All subjects had been previously scanned for indications other than airway pathology and the airway was confirmed to be normal prior to inclusion of data. The replicas were 3D printed (Objet Eden 350V; Stratasys Ltd., MN, USA) using a rigid opaque photopolymer material (VeroGray; Stratasys Lt., MN, USA). Further details on the fabrication of the replicas can be found in the work by Paxman et al.[25] For the present study, branching airways downstream of the carina were removed from the replicas, and 3D printed adapters were attached to the exit of each replica to standard 22 mm breathing circuit tubing. Demographic data and geometric properties of the replicas are presented in Table 1.

Experimental apparatus

A lung simulator (ASL 5000 Breathing Simulator; IngMar Medical, Pittsburgh, PA, USA) was used to simulate tidal breathing through the replicas.

For the present study, breathing frequency (f) and inspiratory/expiratory (i/e) ratio were fixed at 17 breaths per minute (BPM) and 0.85, respectively. Tidal volume (V_t) was fixed at 10 mL/kg body weight yielding a range of 160-245 mL. These breathing parameters were selected as typical in studies involving high

Table 1 Demographic and geometric data for airway replicas used in the present study

Subject number	Age	Sex	Height (m)	Weight (kg)	Airway volume (mL)	Area of nostrils (mm^2)
2	5	M	1.17	22.9	40.4	55
3	5	M	1.12	20.0	35.1	115
5	6	F	1.12	18.0	19.1	85
6	6	F	1.18	21.5	32.1	66
9	5	M	1.13	20.0	21.0	80
10	4	F	0.99	16.0	19.2	58
11	8	M	1.25	24.5	48.4	100
12	6	F	1.24	24.0	22.2	86
13	7	F	1.21	20.0	32.5	84
14	4	F	1.00	16.0	18.6	56

flow and CPAP delivery to children in this age group.[26-28] With these three parameters, the inspiratory and expiratory phases of a breath were modeled as half-sine waves with no inspiratory or expiratory pause.

For tracheal pressures, the intervention, either CPAP or NHF, was applied to the replica which was connected to the lung simulator through standard 22 mm breathing circuit tubing (Figure 3). The length of tubing was kept short to minimize pressure losses and measured 17.0 cm.

For $EtCO_2$, an intervention was applied to the replica, which was connected to the lung simulator through two airway adapters and a static mixer (Figure 4). A capnograph (EMMA Capnograph; Masimo, Irvine, CA) was attached to the adult/pediatric EMMA Airway Adapter (Masimo, Irvine, CA), positioned between the replica and mixer, to measure $EtCO_2$ through infrared spectroscopy. The resulting $EtCO_2$ was displayed as a running average on the screen of the capnograph in mmHg along with the respiratory rate. A straight connector with 7.6 mm port (1964000; Intersurgical, Wokingham, Berkshire, UK) was positioned between the mixer and lung simulator, and used for injection of CO_2. The mixer was used to ensure that the supplied CO_2 was well mixed in the breathing circuit before reaching the capnograph.[29] The internal volume of the connection between the replica and the lung simulator measured 59.2 mL.

A constant flow of 100% CO_2 was bled inline to achieve 5% $EtCO_2$ as a baseline during simulated breathing through each replica without any intervention applied. $EtCO_2$ was converted from mmHg to % CO_2 at an average atmospheric pressure of 707.32 mmHg (Edmonton, Alberta, Canada) over the testing period of the experiments. The required CO_2 injection rates ranged from 60 to 130 mL/min depending on the replica, and are displayed in Table 2. $EtCO_2$ values measured during each tested intervention were reported as a change in % CO_2 from baseline.

Nasal high flow

NHF was delivered with a humidified Nasal High Flow system, Airvo 2, which was provided by Fisher & Paykel Healthcare (Auckland, New Zealand). During the study, the supplied flow was set at a flow rate of 20 L/min, consistent with the flow rate used in studies by McGinley et al. and Amaddeo et al. that investigated NHF for treating OSA in children with a similar age range as the present study.[20,21] Temperature was set at 34°C with supplied oxygen concentration set at 21%. Three high flow nasal cannulas were tested, which were provided by Fisher & Paykel Healthcare: the Optiflow 3S Nasal Cannula (small, OPT1042), the Optiflow+ Nasal Cannula (small, OPT942), and the Optiflow Junior 2 Nasal Interface (XL, OJR418). The inner and outer diameters for each nasal cannula prong are provided in Table 3.

During administration of NHF, PEEP is generated in the upper airway as supplied flow from the cannula reverses direction and exits the airway around the obstruction created by the presence of the nasal prongs positioned in the nares. In fluid mechanics, pressure losses due to obstructions are commonly modeled as minor losses, and may be correlated with Reynolds number (Re).[30] Therefore, the correlation between a minor loss coefficient (K) associated with PEEP and Reynolds number was evaluated. Re was calculated using the leak flow through the characteristic air speed through the non-occluded nares area (U), determined by the flow rate (Q) divided by the area between the nostril walls and the outer wall of the cannula prongs ($A_{non\text{-}occluded}$):

$$U = \frac{Q}{A_{non\text{-}occluded}}$$

The hydraulic diameter (D_h) was calculated by treating the area between the nostril walls and the outer wall of the cannula prongs as an annular cross-section:

$$D_h = D_{OD} - D_{ID}$$

where the inner diameter of the nostril wall is D_{OD} and the outer diameter of the prong is D_{ID}. With these definitions of U and D_h, Re was:

$$Re = \frac{\rho U D_h}{\mu}$$

where density of air (ρ) at 34°C was 1.15 kg/m^3 and dynamic viscosity (μ) was 1.89E–5 kg/m*s.

A minor loss coefficient associated with PEEP was then calculated as:

$$K = \frac{2(PEEP)}{\rho U^2}$$

Continuous positive airway pressure

CPAP was delivered using a CPAP machine (S8 Elite; ResMed, San Diego, CA, USA) connected to a nasal mask (Infant Pocket

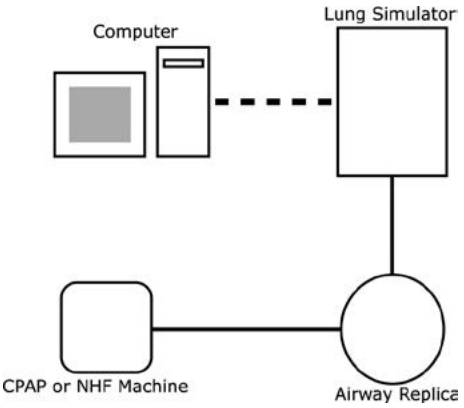

Fig. 3 Schematic of experimental apparatus for measuring tracheal pressures

Mask; nSpire Health Inc., CO, USA) through supply tubing including an exhalation port (Wisp tube and elbow assembly; Philips Respironics, Murrysville, PA, USA). Masks were sealed to the face of each child replica using silicone adhesive. A Pitot tube flow sensor (RespEQ, Baltimore, MD, USA)[31] was attached inline between the CPAP machine and the mask to measure the air flow in real time in standard litres per min ute (SLPM; with standard conditions defined as 21.1°C and 101.3 kPa). SLPM was converted to L/min during analysis using average conditions of the lab during the testing period (21.1°C and 94.3 kPa; Edmonton, Alberta, Canada). The flow waveform was used to calculate the leak flow through the exhalation port, averaged over the breathing cycle, and to ensure that unintended mask leak was at a minimum. This mask leak measurement system was validated and used in a previous study by Duong et al.[16] Two CPAP settings were selected for testing: 5 cmH_2O and 10 cmH_2O. These settings coincide with typical settings used for children of this age range.[20]

Study design

The study was done in two parts, one for assessing tracheal pressures and one for assessing $EtCO_2$.

For tracheal pressures, CPAP settings of 5 and 10 cm H_2O were tested for all 10 replicas. For NHF, the Optiflow Junior 2 nasal cannula was tested in all 10 replicas, but the Optiflow 3S and Optiflow + nasal cannulas were only tested in five replicas (subjects 3, 5, 11, 12, and 13), as prong sizes were too large to fit the nostrils of the other five replicas. A single test ran for approximately 30 breaths while tracheal pressures were recorded by the lung simulator. The pressures were each averaged over five breaths, breaths 21-25, and were used for further analysis. Each intervention was tested three times for each replica, and the NHF cannula prongs were repositioned between repetitions.

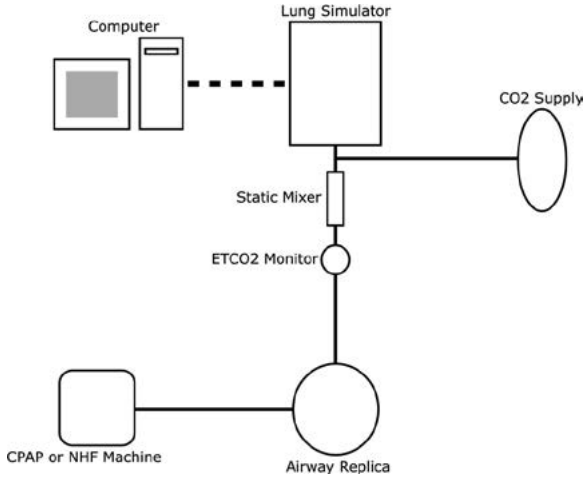

Fig. 4 Schematic of experimental apparatus for measuring $EtCO_2$

Table 2 Tidal volume and CO_2 injection rates for each airway replica

Subject number	Tidal volume (mL)	CO_2 injection rate (mL/min)
2	229	115
3	200	95
5	180	80
6	215	100
9	200	95
10	160	60
11	245	130
12	240	130
13	200	85
14	160	60

For $EtCO_2$, three CPAP settings were tested for all 10 replicas: 5 cmH_2O, 10 cmH_2O, and zero CPAP (with the sealed mask in place). For NHF, similar to the pressure tests, the Optiflow Junior 2 was tested for all 10 replicas, but the Optiflow 3S and Optiflow+ were tested for five replicas. A single test ran until $EtCO_2$ reached steady state and was recorded, typically taking ~80 to 100 breaths. Again, each intervention was tested three times for each replica, and the NHF cannula prongs were repositioned between repetitions.

Statistical analysis

A set of one factor repeated measures Analysis of Variance (ANOVA) procedures were done along with Tukey post hoc analysis comparing the tracheal pressures and change in $EtCO_2$ between CPAP and NHF (n= 10). Three interventions were compared for the four tracheal pressure parameters: 5 cmH_2O CPAP, 10 cmH_2O CPAP, and the Optiflow Junior 2. Four interventions were compared for change in $EtCO_2$: zero CPAP (sealed mask), 5 cmH_2O CPAP, 10 cmH_2O CPAP, and the Optiflow Junior 2. Results with two-sided $P \leq 0.05$ was considered significant.

Another set of one factor repeated measures Analysis of Variance (ANOVA) procedures were done along with Tukey post hoc analysis comparing the tracheal pressures and change in $EtCO_2$ between the three NHF cannulas (n= 5). Three interventions were compared for the four tracheal pressure parameters and change in $EtCO_2$: the Optiflow 3S, the Optiflow+, and the Optiflow Junior 2. Results with two-sided $P \leq 0.05$ were considered significant. Statistical analysis was performed with

Table 3 Inner and outer diameters of nasal cannula prongs

Nasal cannula	Diameter (mm)	
	Inner	Outer
Optiflow 3S	4.2	5.0
Optiflow +	4.1	4.9
Optiflow Junior 2	3.0	3.8

MATLAB (MathWorks, Natick, MA, USA). Tabulated results of all statistical tests performed are available as Additional file 1.

Results

Comparison of CPAP vs NHF

The delivered flow rate of air during CPAP, averaged over the breath, was measured as 18.8 ± 1.1 L/ min for 5 cmH_2O and 26.1 ± 1.6 L/min for 10 cmH_2O (mean±standard deviation; n= 10 replicas).

Average PEEP, PEP, MIP, and AIP across the 10 replicas for the three intervention types are displayed in Figure 5. From ANOVA, the selection between CPAP and NHF was observed to have a significant influence on tracheal pressures. From post hoc analysis, 5 cmH_2O CPAP was different from 10 cmH_2O CPAP for all four pressure parameters, but different from NHF only in terms of PEP and MIP. 10 cmH_2O CPAP was different from NHF in terms of PEEP, MIP, and AIP. Sample pressure waveforms for all individual replicas during administration of CPAP and NHF are displayed in Figure 6.

Average change in $EtCO_2$ from baseline across the 10 replicas for the four intervention types are displayed in Figure 7. Selection between CPAP and NHF was observed to have a significant influence on change in $EtCO_2$. From post hoc analysis, all interventions tested were different from one another in terms of average change in $EtCO_2$, except for the pairing of zero CPAP (with the sealed mask in place) and 5 cmH_2O CPAP.

Comparison between three NHF cannulas

Average PEEP, PEP, MIP, and AIP across the five replicas tested with three different NHF cannulas are displayed in Figure 8. From ANOVA, the selection of nasal cannula was not observed to have a statistically significant influence on tracheal pressures. Sample pressure waveforms for the five tested replicas during administration of NHF for all three nasal cannulas are displayed in Figure 9.

Average change in $EtCO_2$ from baseline across the five tested replicas for NHF are displayed in Figure 10. Similar to tracheal pressures, selection of nasal cannula was not observed to have a statistically significant influence on change in $EtCO_2$.

Minor loss coefficients and Reynolds numbers

Across the three NHF cannulas and ten replicas, the Reynolds numbers calculated using Eq. 3 ranged from 950 to 1350. Minor loss coefficients calculated using Eq. 4 for the Optiflow 3S and Optiflow+ cannulas, and averaged over five replicas, were 23 ± 4 and 20 ± 5, respectively (average±standard deviation). The minor loss coefficient for the Optiflow Junior 2 cannula, averaged over the larger set of ten replicas, was 23 ± 13.

Figure 6 Tracheal pressure waveforms measured over 5 breaths during administration of 5 cmH_2O CPAP (top), 10 cmH_2O CPAP (middle), and NHF at 20 L/min (Optiflow Junior 2 cannula; bottom)

Discussion

Results of in vitro experiments evaluating tracheal pressures and $EtCO_2$ during delivery of CPAP or NHF to child airway replicas are reported above. Several differences between CPAP and NHF warrant further discussion, as do the potential sources of variability in pressure and gas washout between airway replicas.

For the delivery of CPAP, PEEP was observed to be approximately constant across the 10 airway replicas at either 5 cmH_2O or 10 cmH_2O (Figure 5), indicating that the CPAP machine was working as intended, and delivered targeted positive airway pressures. In contrast, PEP, MIP, and AIP were observed to vary between replicas, indicating that these three pressure parameters were influenced by additional factors including breathing flow rates and the airway geometries of each subject (Figs. 5 and 6). This was expected, as airway pressure was evaluated at the exit of each replica (representative of a tracheal pressure), such that pressure drop through the replica influenced the airway pressure in all cases where flow was nonzero. In contrast, PEEP was measured at a point on the breathing cycle of zero flow, such that the instantaneous pressure drop through the replica is also zero.

Unlike the CPAP machine, the NHF system does not adjust delivered flow rate to maintain a constant pressure. As such, all pressure parameters, including PEEP, were observed to be variable across the 10 airway replicas for the delivery of NHF, with negative pressures observed during inhalation for 3 of 10

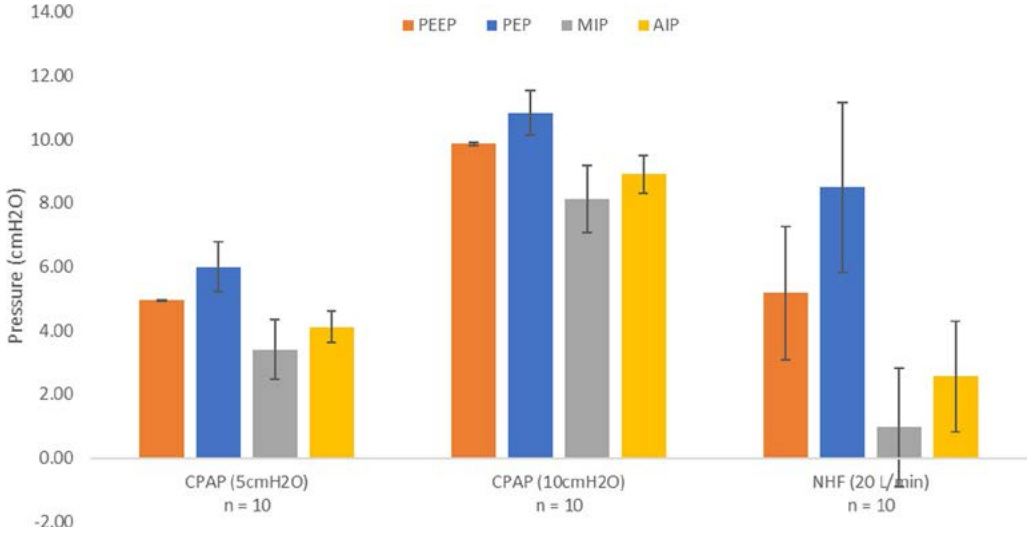

Fig. 5 Average tracheal pressures across all 10 airway replicas for CPAP at 5cmH_2O, CPAP at 10cmH_2O, and NHF at 20 L/min (Optiflow Junior 2 cannula). Error bars represent one standard deviation around the average. *PEEP* positive end-expiratory pressure; *PEP* peak expiratory pressure; *MIP* minimum inspiratory pressure; *AIP* average inspiratory pressure

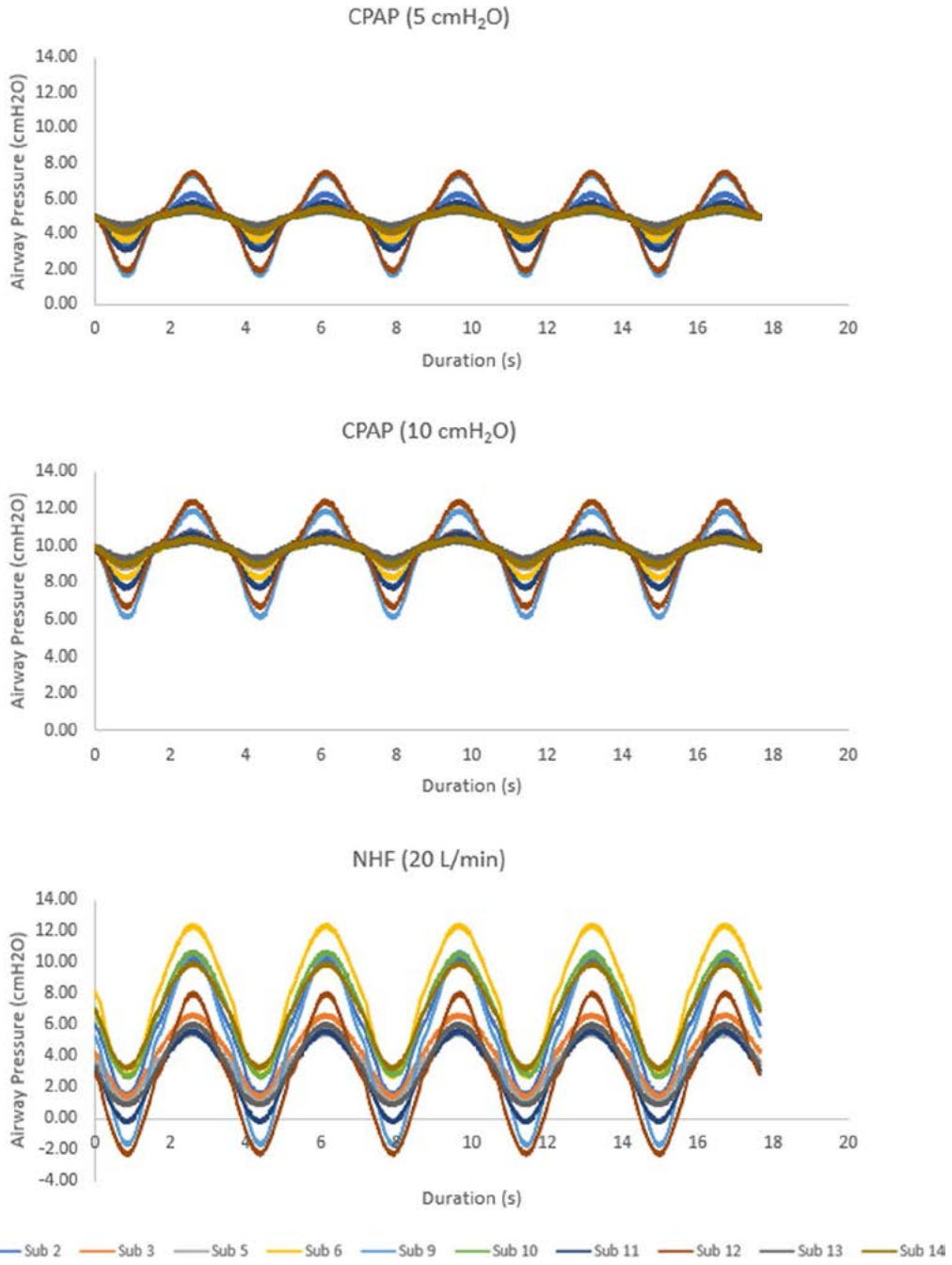

Fig. 6 Tracheal pressure waveforms measured over 5 breaths during administration of 5 cmH_2O CPAP (top), 10 cmH_2O CPAP (middle), and NHF at 20 L/min (Optiflow Junior 2 cannula; bottom)

replicas (Figs. 5 and 6). With a set flow rate of 20 L/min, the average PEEP across the 10 airway replicas was approximately 5 cmH_2O, which is similar to a CPAP setting of 5 cmH_2O. Accordingly, though NHF can generate positive airway pressures, the pressures are variable and subject-dependent. McGinley et al.[20] reported on the delivery of NHF as an alterative to CPAP for children aged 10 ± 1 years (mean±SEM; n= 12) at a set flow rate of 20 L/min. In their study, they found similar reductions in apnea-hypopnea index, comparable to CPAP prior to the study, when using NHF in a majority of the children studied.[20] Prior to NHF, the average CPAP setting used for therapy was 9 ± 1 cmH_2O (mean±SEM; n= 10).[20]

An increase in $EtCO_2$ from baseline was observed during CPAP therapy across all 10 upper airway replicas. The presence of a mask increased $EtCO_2$, due to added dead space of the mask. This increase was smallest for CPAP at 10 cmH_2O (Figure 7), owing to the greater average flow rate delivered from the CPAP machine at the higher CPAP setting. In contrast, a reduction in $EtCO_2$ from baseline was observed during NHF therapy across all 10 upper airway replicas. This is consistent with a known mechanism of NHF: washout of the nasopharyngeal dead space, leading to reduced rebreathing of expired air.[24,32] It is notable that, due to differences between the NHF cannula interface and CPAP mask interface, effective washout was observed for NHF at a flow rate of 20 L/min, whereas no, or limited, washout was observed for CPAP with an average delivered flow rate of 18.8 L/min (for CPAP at 5 cmH_2O), or 26.1 L/min (10 cmH_2O). During exhalation, any flow delivered by the CPAP machine is diverted through the

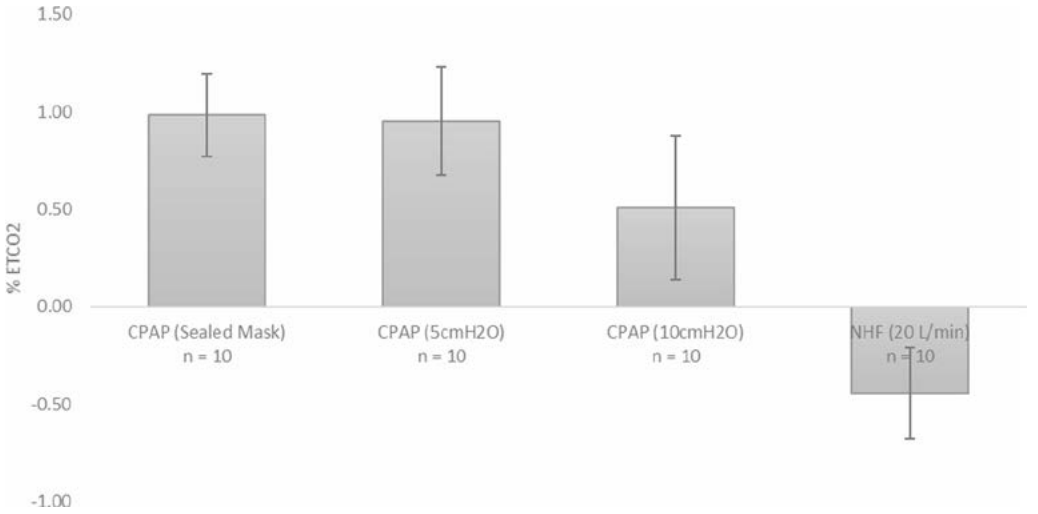

Fig. 7 Average change in %EtCO_2 from baseline across all 10 airway replicas for CPAP with sealed mask on (but zero CPAP applied), CPAP at 5cmH_2O, CPAP at 10cmH_2O, and NHF at 20 L/min (Optiflow Junior 2 cannula). Error bars represent one standard deviation around the average

exhalation port, such that little mixing occurs with gases in the mask or upper airway.

No significant difference was observed in tracheal pressures nor change in EtCO_2 between the three different NHF cannulas for the subset of five tested replicas. An average PEEP of 5.4 ± 1.6 cmH_2O, 4.3 ± 1.5 cmH_2O, and 3.5 ± 0.5 cmH_2O were generated through the Optiflow 3S, +, and Junior 2 nasal cannula, respectively (Figure 8). Though not statistically significant, differences in average PEEP between cannula models may be associated with different cannula prong sizes, as has been noted to influence PEEP in previous studies.[33,34] All three nasal cannulas also had similar reductions in EtCO_2 from baseline: – 0.5 ± 0.3% for the Optiflow 3S, – 0.4 ± 0.2% for the Optiflow+, and – 0.4 ± 0.2% for the Optiflow Junior 2 (Figure 10). However, only five replicas were tested because two of the three nasal cannula models, the Optiflow 3S and the Optiflow+, did not fit the five remaining replicas. This indicates that the selection of nasal cannula for NHF is important for fit and preventing blockage of the nares during delivery of therapy. Relationships between reduction in EtCO_2 from baseline with tidal volume and replica volume were also investigated; however, no correlation was observed. It may be that variability in gas washout during NHF was influenced by the shape of the replica airways, especially the nasal vestibule in immediate proximity of cannula prongs; however, this was not investigated in detail in the present study.

The increased variability between replicas in tracheal pressures generated during NHF as compared to CPAP is noticeable in Figures 5 and 6. Variability in PEEP between replicas was accounted for in part by modeling the pressure drop through the annular space between the prongs and nostril walls as a minor loss. Such a model is frequently adopted in fluid mechanics to calculate the pressure drop associated with flow through a constriction or past an obstruction. On average, calculated minor loss coefficients did not vary appreciably between the three NHF cannulas studied. Furthermore, minor loss coefficients remained approximately constant across the range of Reynolds numbers studied (Re = 950-1350), as is typically observed for flow through a constriction.[30] Similarly, Katz et al.[35] previously adopted a minor loss model for the pressure drop through extrathoracic

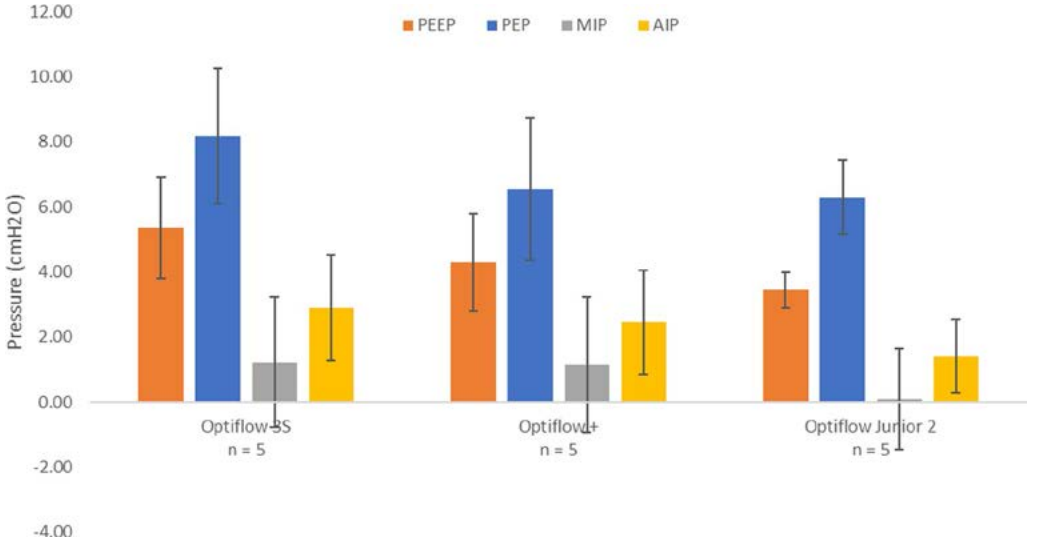

Fig. 8 Average tracheal pressures across 5 airway replicas for three NHF cannulas, Optiflow 3S, Optiflow +, and Optiflow Junior 2. Error bars represent one standard deviation around the average. *PEEP* positive end-expiratory pressure; *PEP* peak expiratory pressure; *MIP* minimum inspiratory pressure; *AIP* average inspiratory pressure

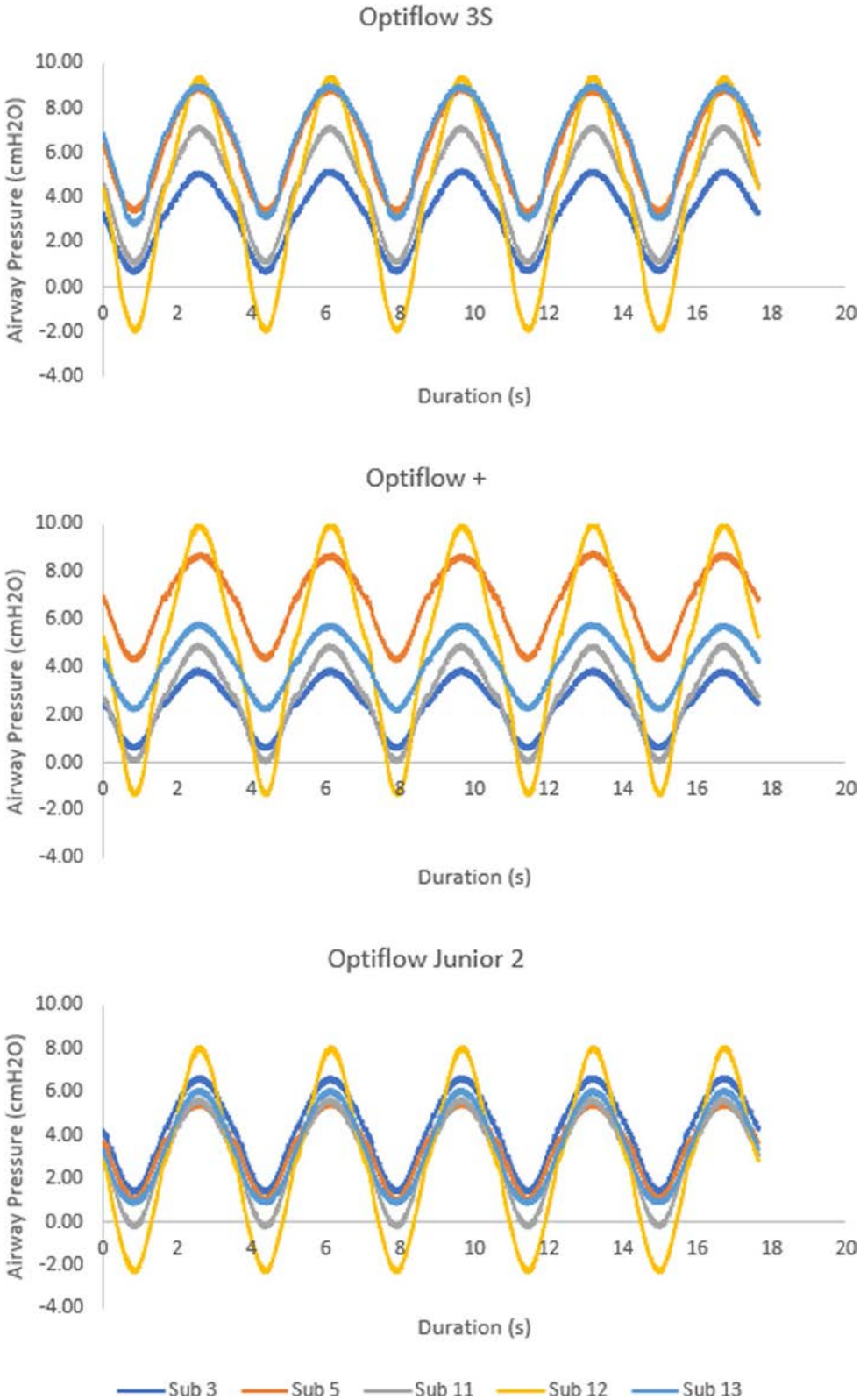

Fig. 9 Tracheal pressure waveforms measured over 5 breaths during administration of NHF using the Optiflow 3S cannula (top), the Optiflow + cannula (middle), and the Optiflow Junior 2 cannula (bottom)

and bronchial airways, and observed that minor loss coefficients approached constant values as Reynolds numbers exceeded ~1000. In the present work, this relationship suggests that PEEP generated in the replicas by NHF was related primarily to the occlusion of the nares by the cannula prongs. For a fixed flow rate of gas supplied to the cannula, the greater the extent of occlusion, the larger the PEEP that will be generated.[36]

Some variability in calculated minor loss coefficients persisted between replicas, and can be attributed primarily to the dissimilar shape of the annular space for different replicas, which is not fully accounted for in the use of a single length scale, namely the hydraulic diameter calculated in Eq. 2. Variation in the percentage of the nostrils' inlet area occluded by cannula prongs may also have contributed to variability between

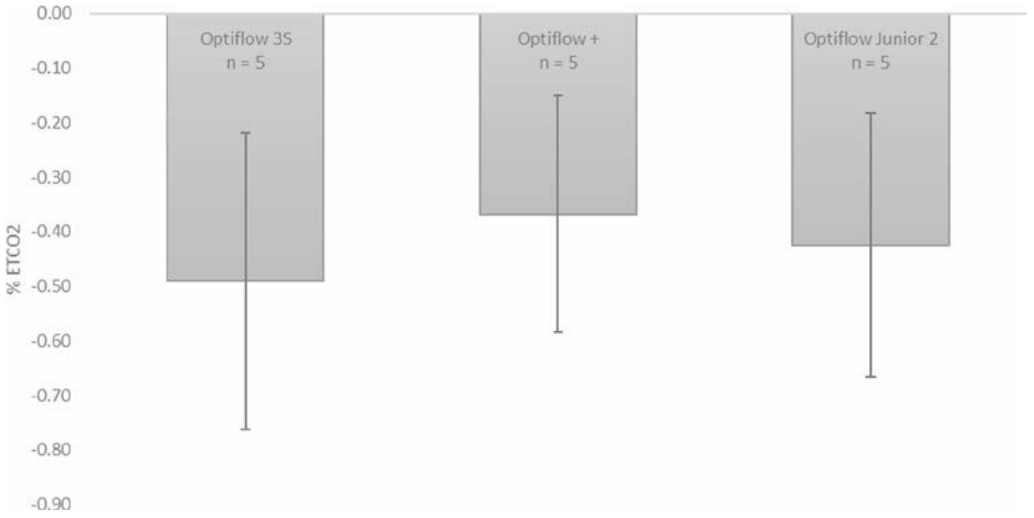

Fig. 10 Average change in %$EtCO_2$ from baseline across 5 airway replicas for the three NHF cannulas. Error bars represent one standard deviation around the average

replicas in the minor loss coefficients. The greater variability in minor loss coefficient between replicas for the Optiflow Junior 2 cannula, as compared with the other two NHF cannulas studied, likely resulted from the larger number of replicas investigated with this cannula. For the subset of five replicas tested with all three NHF cannulas, the percent of occlusion ranged from 34 to 47% for the Optiflow 3S, 33-45% for the Optiflow +, and 20-27% for the Optiflow Junior 2. When tested over the larger set of 10 replicas, the percent of occlusion ranged from 20 to 41% for the Optiflow Junior 2.

Previously, Moore et al.[33,34] identified predictive correlations for PEEP generated during application of NHF based on a characteristic air speed through the non-occluded nares area, as in Eq. 1 of the present study, but also influenced by an additional characteristic air speed exiting the cannula prongs. In the present work, consideration of this additional characteristic air speed did not further improve our ability to account for variability in PEEP between nasal cannulas. This may in part be due to the limited range of air speeds exiting cannula prongs in the present study, which was conducted with a single flow rate supplied to nasal cannula. Furthermore, the Moore et al. studies included high flow nasal cannula from a different manufacturer, which are intentionally designed with smaller inner diameters to influence washout of the upper airway.[37]

A limitation of this study is the use of rigid airway replicas. They did not deform during breathing or under positive airway pressures, and thus the dynamic effects of breathing are not fully captured. Additionally, airway replicas used in the present study were fabricated based on scans of children that were obtained for indications other than airway pathology, whereas children with OSA may have reduced upper airway dimensions compared to controls.[38] We tried to minimize these limitations by testing multiple airway replicas to cover a range of differing airway geometries. Variation in, e.g., airway volume or cross-sectional areas between different airway replicas is expected to be much greater than variation that occurs dynamically over an individual's breathing cycle. Furthermore, the range of airway dimensions measured in children with OSA overlaps that measured in controls,[38] such that we expect the conclusions of the present work to extend to airway geometries representative of children with OSA. A second limitation is the testing of only one flow rate setting for NHF, 20 L/min, for our airway replicas with a subject age range of 4-8 years old. Previous studies have shown both airway pressures and washout to be flow rate dependent.[33,39] However, clinical studies by McGinley et al. and Amaddeo et al. both used 20 L/min when investigating the use of NHF therapy as a treatment for OSA in children, aged 10 ± 1 years and 8.9 ± 6.2 years respectively.[20,21] In both studies, NHF therapy at 20 L/min had a positive effect in treating OSA.[20,21] Therefore, we focused on NHF at 20 L/min as a clinically-relevant flow rate for children with OSA.

Conclusions

NHF delivered at 20 L/min to 4-8 year old child airway replicas generated average PEEP similar to CPAP at 5 cmH_2O. Variation in PEEP, and in the maximum and minimum airway pressures recorded over the breathing cycle, was greater between airway replicas for NHF than for CPAP. Application of NHF reduced $EtCO_2$ from baseline values, whereas delivery of CPAP through a sealed nasal mask increased $EtCO_2$ from baseline values. NHF may benefit children who are non-compliant to CPAP therapy. Thus, further studies investigating NHF therapy as an alternative to CPAP therapy for treating OSA are warranted. These studies should consider potential beneficial effects of improved gas washout when administering NHF distinctly from the use of NHF to produce positive airway pressure.

Abbreviations

AIP: Average inspiratory pressure; ANOVA: Analysis of variance; CPAP: Continuous positive airway pressure; $EtCO_2$: End-tidal carbon dioxide; MIP: Minimum inspiratory pressure; NHF: Nasal high flow; OSA: Obstructive sleep apnea; PEP: Peak expiratory pressure; PEEP: Positive end-expiratory pressure; SLPM: Standard litres per minute.

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Authors' contributions

KD contributed to the design of the study, the acquisition,

analysis and interpretation of data, and drafted the manuscript. MN, JM, and WF contributed to the design of the study, the interpretation of data, and revised the manuscript.

AM contributed to the conception and design of the study, the analysis and interpretation of data, and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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News…continued from page 39
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Comparison of Consistency, Feasibility, and Convenience of a Novel Compact System for Assessing Lung Volumes and Diffusing Capacity vs Whole Body Plethysmography

Summary of a paper published in ClinicoEconomics and Outcomes Research

In a recently published paper[1] describing a multi-center study, the MiniBox+ was shown to be more feasible (significantly lower failure risk) and more convenient (number of attempts needed plus lower execution costs) than whole body plethysmography ("body box"). In addition, the lung volumes (LV) and diffusion capacity (DLco) measurements taken with the MiniBox+ were shown to be highly consistent with those obtained by the body box.

The Study

The aim of the study was to compare the consistency and feasibility of LV and DLco measurements between the MiniBox+ and body box, together with their economic impact. The primary objective was to compare the failure risk in LV and DLco between the two methods, with secondary objectives to compare their consistency and testing costs.

Measurements were taken in 134 patients with obstructive and restrictive respiratory disorders: 42 asthmatics (32.1%), 47 patients with COPD (35.1%), and 44 with restrictive respiratory disorders (32.8%). The body box used in this study was the Platinum DX Elite by MGC Diagnostics (MedGraphics), USA.

The number of attempts required to achieve the first reliable measurement with each method were calculated for all patients, as well as the corresponding time (in minutes) spent on each test. The cost of measurements obtained with each method was calculated by measuring the time spent by the expert nurse in explaining, demonstrating, and performing the tests, and the time spent by patients (loss of productivity) to perform the test.

The Results

Measurement failure

A total of 26 patients (19.4%) experienced at least one failure with the body box, vs 11 patients (8.21%) with the MiniBox+.

Test	No. failed measurements Body Box	No. failed measurements MiniBox+
DLco	69% (18)	8% (11)
LV (TLC, FEV1, or RV)	19% (5)	0
Both	11.5% (3)	0

Number of attempts and total time spent

The mean number of attempts and the total time spent in taking the first reliable measurements were significantly lower with the MiniBox+, both in the case of success and in the case of failure.

	Body Box	MiniBox+	Mean Difference (95% CI)
No. of attempts	2.8	1.4	- 1.2
Total time (min)	13.9	7.2	- 6.1

Consistency between methods

TLC and DLco values obtained by the two measurement techniques were almost equal, with clinically negligible differences.

Cost per test

The total cost per test was estimated at €87.58 for the body box and €75.11 for the MiniBox+, resulting in a cost reduction of €12.33, primarily due to the saving in productivity loss.

Conclusions

The authors state that the complexity of the procedures plays a critical role in determining the feasibility of the two methods. They concluded that the significantly lower failure risk, as well as lower number of attempts and overall time required for first reliable measurements with the MiniBox+, make it a more feasible and convenient method for clinical practice.

For more information about the MiniBox+ visit www.pulm-one.com or email rt@pulm-one.com.

Reference

1 Dal Negro RW, Turco P, Povero M. Comparison of Consistency, Feasibility, and Convenience of a Novel Compact System for Assessing Lung Volumes and Carbon Monoxide Diffusing Capacity versus Whole Body Plethysmography. Clinicoecon Outcomes Res. 2021; 13: 637–643.

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