understand underlying mechanisms. PFOs had no significant association with survival, although this should be evaluated in a larger study.

Reference

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Machine-learning approach to estimating percentage predicted forced expiratory volume in 1 second in cystic fibrosis using computed tomography-derived lung parenchymal biomarkers

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Background: Computed tomography (CT) attenuation patterns in the lung become more complex with disease progression in people with cystic fibrosis (PwCF) because of chronic inflammation of lung parenchyma [1]. Although pulmonary function tests (PFTs) are the gold standard for monitoring lung disease in CF, some studies have demonstrated that CT-based radiology scores can detect changes earlier than PFT, suggesting CT sensitivity in CF [2], but obtaining radiology scores is time consuming and subjective. Lung parenchymal biomarkers derived from CT image processing are quick and reproducible and have been demonstrated to quantify parenchymal abnormalities [3]. Our central hypothesis was that imaging biomarkers would have translational applications in CF. To test this hypothesis, we developed a machine learning (ML) model to estimate percentage predicted forced expiratory volume in 1 second (FEV1)pp in PwCF using CT-derived lung parenchymal measures alone.

Methods: Lung parenchymal biomarkers describing different components of CT attenuation distribution were derived using an in-house-developed automated program and pyradiomics [4]. Individuals with CT and PFTs within 3 months from our CF center were included. We trained ML regression models using decision trees, random forest, and extreme gradient boosting (XGBoost) to estimate FEV1pp measured using PFT using CT-derived parenchymal measures. The dataset was split 70:30 between training and testing tasks of ML using stratified sampling. Ten-fold cross-validation was used to find the best hyperparameters for each model. Root mean squared error (RMSE) was used to assess ML model performance.

Results: We included 153 PwCF (age 14.3 ± 3.6; 59 male/94 female; FEV1pp as measured by PFT: 82.8 ± 22.8%). ML regression models were trained on 23 of 121 lung parenchymal measures derived from CT scans, after feature selection. The XGBoost regression model performed best in estimating FEV1pp (RMSE 6.4%). The ML model error in FEV1pp is on the same order of repeatability errors in FEV1pp in spirometry reported in the 2012 NIOSH Spirometry Quality Assurance Study.

Conclusions: This study demonstrates that ML models have translational applications in predicting FEV1pp in CF. Future studies will further refine this ML model by including clinical data and demographic characteristics and will eventually deploy the model to inform clinical practice.

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Feasibility of telehealth spirometry for people with cystic fibrosis

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Background: Telemedicine has flourished during the COVID-19 pandemic. There is increasing interest in performing spirometry at home as part of a telehealth program, especially in cystic fibrosis (CF), to follow the course of the disease, but it is unclear whether the quality and accuracy of home spirometry are comparable with those of in-clinic spirometry [1–3]. This study aimed to evaluate the feasibility and measurement quality of telehealth spirometry assessments for people with CF.

Methods: Patients with acceptable hardware at home were provided with a flow sensor portable spirometer (Spirobank Smart) compatible with ATS/ERS 2019 standards for volume accuracy. They performed spirometry during “home admissions” or ongoing home monitoring for 1 year during the COVID-19 pandemic (January 2021 to January 2022). At the end of each session, the family forwarded the data to the CF center.

Results: Twenty-nine people were evaluated (median age 17.4, range 6.7–34; 58% female; mean baseline percentage predicted forced expiratory volume in 1 second 79.8 ± 21.4%). According to American Thoracic Society/European Respiratory Society criteria, spirometry was performed successfully in 320 of 430 (74.5%) attempted sessions. The median distance between the subject’s home and the hospital was 124 km (range 49–418 km)—a median travel time saving of 1.5 hours per hospital visit.

Conclusions: Home-based telehealth spirometry is feasible in people with CF and can support the CF team in ongoing outpatient monitoring.

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Respiratory symptom changes during menstrual cycles in women with cystic fibrosis

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Background: Women with cystic fibrosis (WwCF) have worse outcomes than their male counterparts. After puberty, WwCF have higher rates of pulmonary exacerbations, faster decline in lung function, and poorer nutrition [1]. The etiology of this gender gap is unclear and probably multifactorial: given the estrogen and progesterone receptors in lung tissue, sex hormones and their changes play a role. Inflammatory lung biomarkers and lung function fluctuate during the menstrual cycle of WwCF [2]. With this study, we aimed to determine changes in respiratory symptoms in WwCF throughout their menstrual cycle.

Methods: We included WwCF with regular menstrual cycles who were not taking any hormonal contraceptives. Participants notified the investigator...
when their menstrual cycle started and were sent RedCap surveys to assess respiratory symptoms at different menstrual cycle phases over a 6-month period. Time points correlated with the different phases of the menstrual cycle: day 1 (start of follicular phase, menstrual period), day 13 (ovulation phase), and day 21 (luteal phase). Ten symptoms were evaluated to calculate a Respiratory Symptom Menstrual Cycle (RSMC) score. Self-reported symptoms were compared with their subjective baseline; improved from baseline (−1); at baseline (0); and mildly (1), moderately (2), and severely increased from baseline (3). Total symptom scores ranged from −10 to 30. We determined changes in RSMC score between points in their cycles and constructed a mixed-effects linear regression model to explore the association between menstrual cycle day (13 vs 21 vs 1) and total symptom score (dependent variable, RSMC score; independent variable, menstrual cycle day; random effect, patient).

Results: Despite multiple contact attempts, only seven of 13 WwCF who provided consent completed at least three surveys. We analyzed data from these 7 patients. Participants were aged 20 to 45 and had a mean body mass index of 22.6 kg/m² and mean percentage predicted forced expiratory volume in 1 second of 71.5%, all had chronic Pseudomonas infection, 86% had at least one copy of F508del, and 86% were on highly effective modulator therapy (HEMT). The most common reported symptom changes were cough, sputum, and overall sputum quality, each reported in 57% of patients. There was a large variation in overall RSMC scores across participants, with no clear worsening for the cohort at any point in the cycle. There was no statistical association between day and RSMC score when each day was compared with day 1, day 13, or day 22 (day 13 vs day 1, regression coefficient 0.00, 95% CI, −1.77–1.77, p > 0.09; day 21 vs day 1, regression coefficient −0.41, 95% CI, −2.15–1.32, p = 0.64) (Figure 1).

Conclusions: Our results show that there is large variation in RSMC scores between WwCF, with no association between RSMC score and different time points of the menstrual cycle. Poor survey response, resulting in a small sample size, limited our study. Most patients had been started on HEMT, which decreased their overall respiratory symptoms. Online surveys may not be the best way to engage participants; tracker phone applications may be a better option for several cycles. Larger studies are needed to evaluate the impact of sex hormones on respiratory symptoms and other physiologic parameters in WwCF to understand better the gender gap.

References


**133 Clinical response to elixacaftor/tezacaftor/ivacaftor in people with cystic fibrosis with the N1303K and non-modulator responsive mutation**

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**Background:** Significant improvement in lung function, nutritional status, quality of life, and sweat chloride test results was shown in people with the F508del cystic fibrosis (CF) transmembrane conductance regulator (CFTR) mutation treated with elixacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) [1–3]. In 2019, the Food and Drug Administration approved the use of ELX/TEZ/IVA for those patients, and the label was recently expanded for people with at least one of the responsive misprocessing CFTR mutations [4], not including the N1303K, a class II mutation associated with abnormal CFTR processing. The N1303K-CFTR protein fails to undergo complex glycosylation, leading to cytoplasmic degradation with no or minimal function of CFTR. For people with the N1303K mutation, recent in vitro analysis with patient-derived nasal epithelial cell culture showed a significant increase in CFTR function after 48 hours of treatment with ELX/TEZ/IVA, although there was negligible improvement in CFTR protein processing, suggesting that potentiation of the function of membrane residual CFTR proteins, and not improved protein processing, caused the increase in function [5].

**Methods:** Seven people with CF aged 9 to 39, one N1303K homozygous, six compound heterozygous for N1303K, three with W1282X, one with E884G, one with G542X, and one with 3121+1A>G started off-label treatment with ELX/TEZ/IVA.

**Results:** Significant clinical improvement was demonstrated in all participants shortly after initiation of ELX/TEZ/IVA. On average, mean forced expiratory volume in 1 second (FEV1) increased by 20.7 percentage points (from 73.0% to 93.7%; 95% CI, 10–30, p < 0.01), mean weight increased by 2 kg (from 47.9 kg to 49.9 kg; 95% CI, 1–3, p < 0.01), mean lung clearance index (LCI) decreased by 4.1 (from 16.1 to 12; 95% CI, −0.4–8.5, p < 0.03). There was no significant change in sweat chloride tests. All patients reported dramatic improvement in general well-being and significant reduction in sputum production.

**Figure 1.** Respiratory symptom menstrual cycle total score stratified according to patient at days 1, 13, and 22 of their menstrual cycle.