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Pre-procedural Sars-CoV-2 testing and pulmonary function testing

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Background: CF Foundation guidelines encourage quarterly pulmonary function testing (PFTs) for all patients as part of routine care. The COVID-19 pandemic significantly affected our ability to obtain PFTs at recommended intervals, as patients were reluctant to come to the hospital and being advised to shelter in place to avoid unnecessary exposure to the Sars-CoV-2 virus. To obtain PFTs at our center during this time, we required negative Sars-CoV-2 testing for asymptomatic patients in the preceding 48–72 hours. We hypothesized that the extra trip away from home for viral testing affected our ability to adhere to the recommended PFT testing intervals. We sought to analyze the number of patients who did not have any PFTs completed since the start of the testing requirement. We also sought to analyze the positivity rate for Sars-CoV-2 associated with PFTs.
Methods: All charts of CF patients ordered for PFTs and Sars-CoV-2 PCR testing from July 2020 to March 2021 were retrospectively queried for viral test results and either the subsequent completion or cancelation of a PFT appointment. Charts were abstracted for patient age, number of PFTs completed, and Sars-CoV-2 status.
Results: Patient ages ranged from 6 years to 55 years. Of the 110 patients, 37 (34%) were under 18 years old. PFTs were ordered 134 times on 110 patients during the 9-month period, along with antecedent viral testing. Thirty-five patients (32%) did not have any PFTs completed in that time frame. None of the viral testing for Sars-CoV-2 prior to each PFT returned positive (0%). Nine patients (9%) tested positive independent of their PFT appointments and were tested due to symptoms, only 1 of whom was a pediatric patient.
Conclusion: At our single center of 121 patients, we found a 0% positivity rate of Sars-CoV-2 PCR in asymptomatic CF patients preparing for PFTs. We also found that since the implementation of this extra testing requirement, nearly one-third of our patients did not have any PFTs during the pandemic. With vaccination rates steadily increasing among both hospital staff and CF patients, we believe this low positivity rate argues for the removal of pre-procedural viral testing in this population when asymptomatic, provided that we continue to utilize symptom screening questions, appropriate PPE, and appropriate room cleaning procedures as outlined by the American Thoracic Society. The removal of the pre-procedural viral testing would eliminate a significant barrier to obtaining routine care for our CF patients.

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C-reactive protein (CRP) as a biomarker of exacerbation presentation and treatment response

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Background: C-reactive protein (CRP), a systemic marker of inflammation, has been proposed as a biomarker for pulmonary exacerbation (PEx) diagnosis and treatment response. CRP >75 mg/mL ($\log_{10}$CRP >1.875) has been associated with increased risk of PEx treatment failure. We interrogated CRP measures collected during the STOP2 PEx study (NCT02781610) of clinical response to different intravenous (IV) antimicrobial treatment durations as a PEx presentation and treatment response biomarker.
Methods: The STOP2 study design has been reported in detail [1]. CRP measures were collected at IV antimicrobial treatment start (V1), randomization (V2, 7 to 10 days after treatment start), and 2 weeks post-treatment end (V3) and converted to $\log_{10}$ values. Correlations between V1 $\log_{10}$CRP, $\log_{10}$CRP change from V1 to V3, and clinical responses (change in lung function as $ppFEV_1$ and Chronic Respiratory Infection Symptom Score [CRISS] from V1 to V3) were assessed by least squares regression. Clinical responses associated with V1 $\log_{10}$CRP >1.875 versus ≤ 1.875 mg/L were compared by *t* test. Subjects with covariate data missing at a given visit were excluded only from analyses that included those specific covariates at those visits, without imputation.
Results: In all, 951 (92.7%) of 982 STOP2 subjects had CRP measures at V1. Mean V1 $\log_{10}$CRP varied significantly by lung function subgroup ($ppFEV_1$ < 40, 1.4 [95%CI 1.4, 1.5] vs ≥70, 0.8 [0.7, 0.9]), CRISS quartile (≥59, 1.4 [1.3, 1.5] vs < 44, 0.9 [0.8, 1.0]), and sex (females 1.1 [1.1, 1.2] vs males 1.2 [1.2, 1.3]), but not by age subgroup. V1 $\log_{10}$CRP correlated somewhat with $\log_{10}$CRP change from V1 to V3 ($r^2 = 0.255$) but less so with V1 to V3 changes in ppFEV1 ($r^2 = 0.016$) or CRISS ($r^2 = 0.031$). Correlations of $\log_{10}$CRP changes from V1 to V3 with ppFEV1 and CRISS changes from V1 to V3 were modest (r^2 of 0.061 and 0.066, respectively). In all, 109/951 subjects (11.5%) had a V1 $\log_{10}$CRP >1.875 mg/L; mean V1 to V3 ppFEV1 and CRISS changes were significantly better for this group than those with $\log_{10}$CRP ≤1.875 mg/L ($ppFEV_1$ response of 9.1 [7.0, 11.3] vs 6.1 [5.5, 6.8]; CRISS response of −24.6 [−26.6, −21.6] vs −17.6 [−18.6, −16.6]).
Conclusion: V1 $\log_{10}$CRP concentrations varied widely at PEx diagnosis in the STOP2 study cohort. Correlations between $\log_{10}$CRP concentration changes from V1 to V3 and ppFEV1 and CRISS changes over the same period were very modest, suggesting that CRP change will have limited utility as a biomarker of PEx treatment response. A $\log_{10}$CRP of >75 mg/L at PEx diagnosis did not predict a worse lung function or symptom change from V1 to V3 (in fact, these subjects had significantly better mean treatment responses).

Reference

1. Heltshe *et al. Contemp Clin Trials*. 2018;64:35–40.

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Late diagnosis of cystic fibrosis after first decade of life: Clinical observations of a milder phenotype in India

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Background: There is paucity of data on the prevalence, phenotype, and clinical outcome of patients with cystic fibrosis (CF) from the Indian subcontinent, specifically among those who were diagnosed after the first decade of life. In general, late diagnosis results in severe pulmonary and nutritional morbidity. We report data from a cohort of patients with CF (PwCF) focusing on those with a milder phenotype of CF disease despite late diagnosis.
Methods: Retrospective chart review of PwCF followed at a tertiary medical center in India was conducted. Of the 63 newly diagnosed PwCF between May 2018 and December 2020, 18 were diagnosed after 10 years of age. Patient demographics, clinical outcomes, spirometry, nutritional parameters, and diagnostic data were reviewed.
Results: Of the 18 patients, 11 were from India and 7 from Bangladesh. Median age was 16 years (range 10.5 – 23.4 years) and 10 (56%) were male. Overall, median age at which earliest symptom was reported was 1.9 years (range 0.1–15 years); however median age of diagnosis was 12 years (range 10.25–21.75). In the first decade, the majority did not report any recurrent CF-specific symptoms, and 3 patients reported only fatigue in summer. Sweat chloride levels were diagnostic in 9/18 (50%), in the indeterminate zone in 8, and normal in 1 patient. Family history of CF was noted in 27% of patients. CFTR sequencing with deletion/duplication was completed in 16 patients. None had homozygous F508del mutations; 4 patients were heterozygous for F508del and of these patients, 3 were pancreatic insufficient. Three patients were heterozygous for the intronic variant 3718–2477C >T (previously reported from India); all 3 had normal or indeterminate sweat chloride levels and 2 were pancreatic sufficient. From a pulmonary perspective, 83% had respiratory symptoms with a mean