

## **Occupational and Environmental Lung Diseases**

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## NONINVASIVE BIOMARKERS OF AERODIGESTIVE DISEASE: ENVIRONMENTAL EXPOSURE, RISK AND PHENOTYPIC PROFILE

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**PURPOSE:** The destruction of the World Trade Center (WTC) led to the exposure of first responders and inhabitants of New York City to WTC-particulate matter (WTC-PM) leading to the development of gastroesophageal reflux disease(GERD), Barrett's Esophagus(BE) and airway hyper-reactivity (AHR). Although many studies have suggested interdependence between airway and digestive diseases, the causative factors and specific mechanisms remain unclear. Our work aimed to define and phenotype aerodigestive/gastrointestinal health biomarkers. We leveraged the WTC-exposed cohort to identify novel biomarkers of WTC-aerodigestive disease and develop noninvasive disease phenotyping to promote early diagnosis and treatment.

METHODS: Study Design: a subset of our representative-cohort was contacted. GERD, BE, AHR and controls were defined by clinical, pathological, WTC certification and EMR review. Questionnaires were deployed using REDCap: Health-Related QoL (HRQL), St. George's Respiratory Questionnaire (SGRQ), Short-Form 36 (SF36), Patient Assessment of Gastrointestinal Disorders—Quality of Life(PAGI-QOL) and -Symptom Severity Index (PAGI-SYM). Saliva was collected using PepsinCheck(RD Biomed); 1. AM, 2. 1h after lunch, and 3. Dinner prior to visit. During in-person visits, patients had: serum; Exhaled Breath Condensate (EBC;RTube), pH measured post-deaeration using free argon gas; microbriome with naso- and oropharyngeal swabs (DNA Genotek); spirometry (KOKO; nSpire Health Inc); FeNO (NIOX VERO®; Aerocrine); and cognition (MoCA and MMSE) assessed.

**RESULTS: Demographics:** Subjects screened/enrolled (n=52;REDCap). GERD/BE subjects were more often on proton pump inhibitors (PPIs) and histamine(H)<sub>2</sub> blockers; while AHR subjects were more often on SABAs and PPIs (p<0.05). **Biomarkers:** Positive peptest (>16ng/mL) was seen in 35% of subjects, and salivary pepsin was significantly increased in GERD/BE subjects when compared to either controls or AHR. Lower EBC pH was observed in GERD/BE subjects when compared to controls (p<0.05) and AHR subjects (NS). Higher FeNO levels were observed in subjects with GERD/BE when compared to controls and AHR (NS). PPI-users had a lower EBC pH and higher FeNO levels than non-users (NS). **Questionnaires:** Lower PAGI-QOL and higher PAGI-SYM scores observed in GERD/BE subjects. 20% subjects reported a MoCA score below 26 and 5% had an MMSE score below 24 (cutoffs commonly considered to be abnormal).

**CONCLUSIONS:** Thus far, use of PPI, low EBC pH, and elevated FeNO may identify confounding GERD in subjects with AHR. Further, lower EBC pH and higher FeNO correlated with worse PAGI-SYM and PAGI-QOL scores with a significant correlation observed between FeNO and PAGI-QOL scores. Future studies plan to optimize this noninvasive biomarker model of aerodigestive disease and their longitudinal association using machine learning techniques.

CLINICAL IMPLICATIONS: Aerodigestive complications include AHR, GERD, and premalignant BE. However, studies are limited in clarifying their pathophysiological link. Therefore, discovery of biomarkers of GERD/BE, and the overlap of aerodigestive disease is important to identify populations who may benefit from earlier intervention, targeted therapies, and improve quality of life. Our work will continue to focus on resolving current gaps of knowledge on biomarkers of WTC-aerodigestive disease.

## **DISCLOSURES:**

No relevant relationships by Fritz Francois

Consultant relationship with Medtronic Please note: 2015-present Added 04/04/2024 by Abraham Khan, source=Web Response, value=Consulting fee

Speaker/Speaker's Bureau relationship with Sanofi and Regeneron Please note: 2023-present Added 04/04/2024 by Abraham Khan, source=Web Response, value=Honoraria



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