Objective: Sex discrepancies have been reported in total sino-nasal outcomes test (SNOT-22) but limited data exists on sex differences within SNOT-22 subdomains and tissue biomarkers.

Study Design: Prospective cohort

Setting: Academic medical center

Methods: Patient demographics, mucus swabs and clinical data including SNOT-22 were collected. Sex differences in SNOT-22 subdomains were assessed using linear regression. A random forest model was applied to assess importance of variables in predicting total SNOT-22 score. Enzyme-linked immunosorbent assays (ELISA) were used to measure Substance P and tryptase in a subset of mucus samples from men and women matched for age and disease type to explore biological sex differences and relationship to SNOT-22.

Results: A total 520 patients were studied (mean age 48.3 years, 50.9% female). A statistically significant difference amongst age existed between genders (50.1 years old vs 46.6 years old, p= 0.008). Men had more CRS with nasal polyps (CRSwNP) than women (48.2% vs 35.5%, p= 0.004) while women had more disease without nasal polyps (CRSw/oNP) (34.1% vs 43%, p= 0.046). Men had a higher mean Computed tomography (CT) Lund-Mackay Score (11.3 vs 9.5, p= 0.004) while women had a higher overall mean SNOT-22 score (40.9 vs 46.9, p= 0.001) Regarding SNOT-22 subdomains, women had statistically significant higher scores in ear/facial, psychological and sleep domains (p= <0.0001, 0.0034, 0.0065 respectively). The random forest model revealed age, objective disease measures, sex were top predictors for Total SNOT-22 above other variables such as smoking, presence of comorbid allergy or asthma and presence of polyps or Aspirin Exacerbated Respiratory Disease (AERD). Mucus substance P was not statistically associated with Total SNOT-22 score.

Conclusion: Applying SNOT-22 subdomains may be beneficial in sex focused therapy as clear differences exist in CRS disease manifestations amongst men and women.