Sex Specific Quality of Life Differences in Chronic Rhinosinusitis

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Background

- The use of subdomains in the Sino-Nasal Outcome Test (SNOT-22) has been validated to describe Chronic Rhinosinusitis (CRS) symptoms.
- Sex discrepancies have been reported in total SNOT-22 scores and individual traits, but limited data exist and subdomains have not been reported.
- Tissue biomarkers of CRS in regards to sex have not been assessed.

Hypothesis

- Women preferentially suffer from different CRS-related symptoms and comorbid conditions such as migraine disorder.
- Neuropeptides such as Substance P will be locally elevated in women with CRS.

Methods

- CRS patients presenting to a tertiary care rhinology facility for surgical intervention were recruited into an IRB-approved biobank (Univ of Colorado), where SNOT-22 and middle meatal mucus swabs were obtained.
- Patient demographics and characteristics were summarized by mean (sd) or frequency (%) for the overall cohort and by sex.
- Gender differences in SNOT-22 subdomains were assessed using linear regression and adjusted for age, CRS diagnoses, smoking status, and use of topical nasal saline or corticosteroid medications.
- A random forest (RF) model was applied to assess importance of variables in predicting total SNOT-22 score.
- Significance assessed using two-sample t-tests for continuous variables and chi-square tests of independence or Fishers exact tests for categorical variables.
- Mucus Substance P was measured by ELISA in a subset of men and women matched for age and disease type to explore sex differences and relationship to SNOT-22 quality of life (QOL).
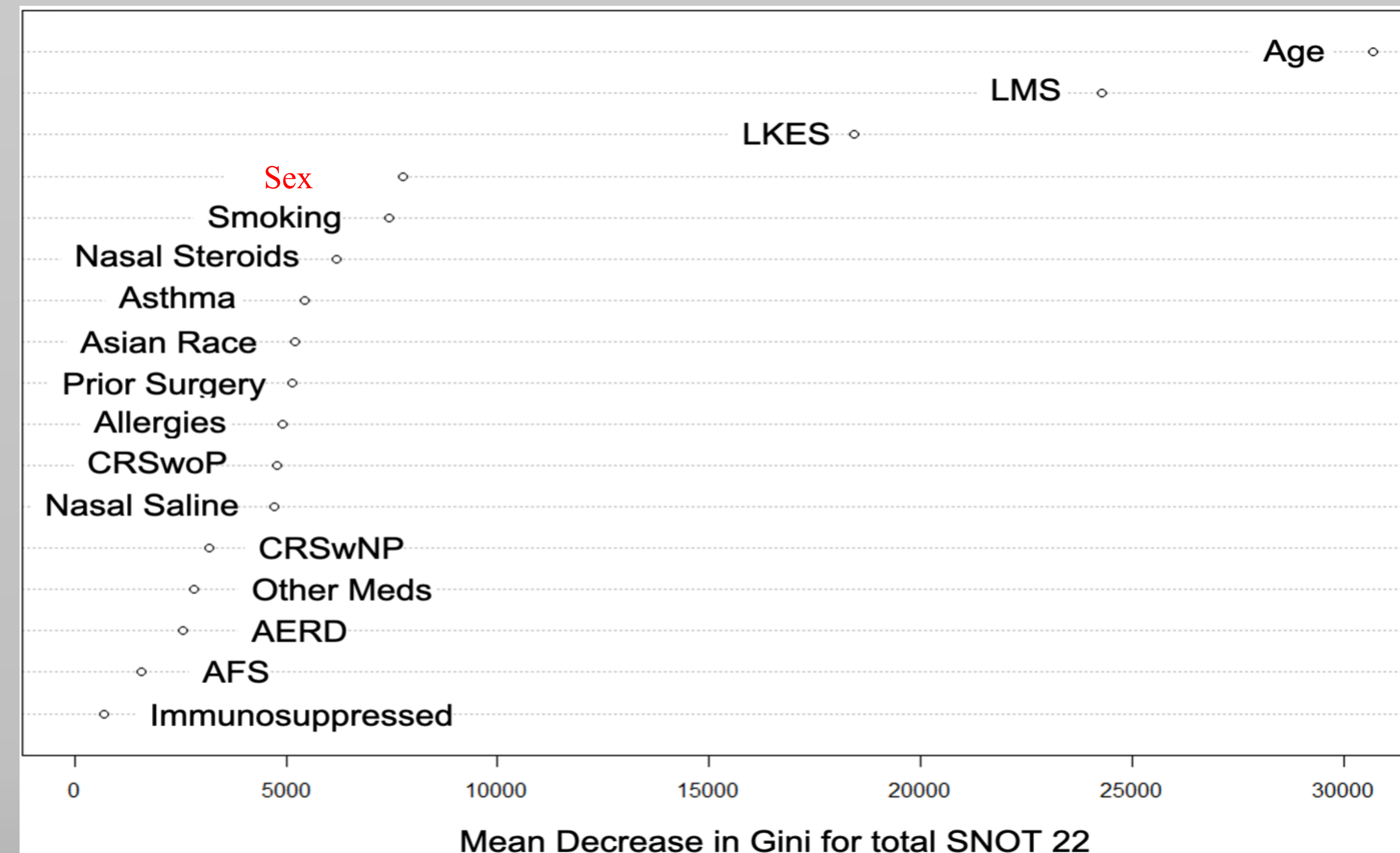
Patient Demographics

Demographics	Mean (SD) N (%)	Mean (SD) N (%)	Mean (SD) N (%)	p-value*
	Overall, N=520	Males, N=255	Females, N=265	
Age (years)	48.3 (15.1)	50.1 (14.8)	46.6 (15.4)	0.0081
Race				
Native American	2 (0.39)	0 (0)	2 (0.76)	
Asian	8 (1.5)	3 (1.2)	5 (1.9)	
Black	28 (5.4)	12 (4.7)	16 (6.0)	
White	436 (83.8)	219 (85.9)	217 (81.9)	
Hispanic	36 (6.9)	18 (7.1)	18 (6.8)	
Other	10 (1.9)	3 (1.2)	7 (2.6)	0.4812

Disease Characteristics

Clinical	Mean (SD) N (%)	Mean (SD) N (%)	Mean (SD) N (%)	p-value*
CRSwNP	217 (41.7)	123 (48.2)	94 (35.5)	0.0042
CRSw/oNP	201 (38.7)	87 (34.1)	114 (43.0)	0.0462
Polyposis with Aspirin Sensitivity	41 (7.9)	18 (7.1)	23 (8.7)	0.6012
AFS	1 (0.19)	1 (0.39)	0 (0)	NA
Immuno_suppresed	10 (1.9)	5 (1.9)	5 (1.9)	1.0000
Allergies[1]	283 (54.4)	137 (53.7)	146 (55.1)	0.9395
Asthma[2]	257 (49.4)	123 (48.2)	134 (50.6)	0.7972
Smoking				
Former	160 (30.8)	89 (34.9)	71 (26.8)	
Current	39 (7.5)	21 (8.2)	18 (6.8)	
Never	321 (61.7)	145 (56.9)	176 (66.4)	0.0767

Treatment	Mean (SD) N (%)	Mean (SD) N (%)	Mean (SD) N (%)	p-value*
Nasal Saline	391 (75.2)	183 (71.8)	208 (78.5)	0.0942
Nasal Steroid	380 (73.1)	176 (69.0)	204 (77.0)	0.0515
Other medical management	37 (7.1)	15 (5.9)	22 (8.3)	0.3669
Previous Surgery	255 (49.0)	122 (47.8)	133 (50.2)	0.7904
Disease Severity				
Endoscopy Score	5.1 (3.9)	5.2 (3.9)	4.9 (3.8)	0.3454
CT Lund-Mackay Score	10.4 (6.8)	11.3 (6.9)	9.5 (6.7)	0.0039
SNOT-22 Score	44.0 (21.3)	40.9 (20.7)	46.9 (21.6)	0.0013

Fig 1: Random Forest Model for Total SNOT-22 Predictors

Mean Decrease in Gini for total SNOT 22

Sex Differences in SNOT-22 Subdomains

SNOT 22 Subscale	Mean (se) difference between sex	p-value
Total	5.1 (1.78)	0.0046
Rhinologic	0.56 (0.59)	0.3433
Extranasal	0.35 (0.31)	0.2594
Ear/Facial	1.97 (0.43)	<0.0001
Psych	1.83 (0.75)	0.0148
Sleep	1.45 (0.62)	0.0192

**Figure 1: Random Forest Model for Total SNOT-22 Predictors**

- Higher values across the mean decrease in Gini index determine which variables are likely to predict higher SNOT-22 scores.

LMS: CT Lund-Mackay Score, LKES: Endoscopy Score

Figure 2: Total SNOT-22 vs Concentration of Substance P by Sex

- Mean concentration of Substance P of 0.23 and 0.19 pg/ul Total Protein in females and males, respectively.
- CI: -0.69, 0.038   p-value: 0.57

Fig 2: Total SNOT-22 Score vs [Sub P] by Sex
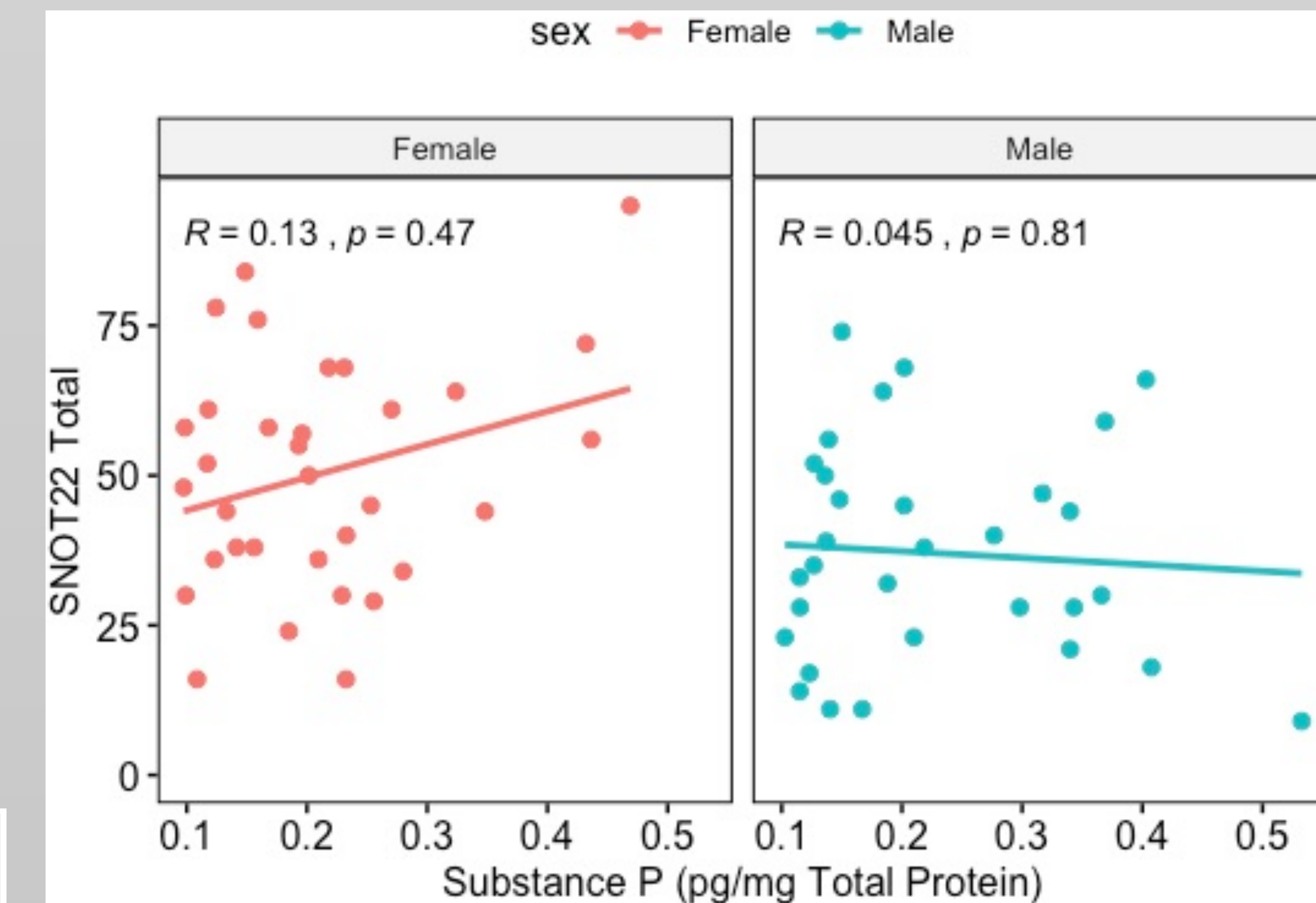
Results

Demographics and Baseline Disease Characteristics

- Significant age difference in male vs female groups with questionable biological importance
- Sex differences in proportion of CRS subject with and without NP

Sex Differences in SNOT-22

- Females suffered a higher QOL burden by total SNOT-22 score, despite similar disease on endoscopy and lesser disease on CT.
- Females exhibited worse QOL in SNOT-22 subdomains of Ear/Facial, Psychology and Sleep.

Random Forest Model for Total SNOT-22 Score

- Top predictors for Total SNOT-22 were age, objective disease measures (CT and endoscopy scores), and then sex, above other variables such as smoking, presence of comorbid allergy or asthma, and presence of polyps or AERD.

Substance P by Sex and SNOT-22 Total

- Mucus Substance P was not statistically associated with Total SNOT-22 score, but exhibits a trend towards a weak association in the female group.

Conclusion

- Sex differences in patients with CRS exist between age at presentation for surgery, total SNOT-22 score, and SNOT-22 subdomain scores.
- Among the many predictor variables for total SNOT-22 score, sex is surprisingly high and warrants further attention.
- Substance P may weakly associate with total SNOT-22 score.

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