Göteborg, 2019

CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

Symptoms, Heredity and Genetics

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinargatan 3, Göteborg, den 20 maj 2019 klockan 09:00.

av
Anton Bohman

Fakultetsopponent:
Professor Martin Desrosiers
Université de Montréal, Kanada

Avhandlingen baseras på följande delarbeten

I. **Bohman A, Oscarsson M, Holmberg K, Johansson L, Millqvist E, Nasic S, Torinsson-Naluai Å, Bende M**. Heredity of nasal polyps. Rhinology. 2015 Mar;53(1):25-8.

II. **Bohman A, Oscarsson M, Holmberg K, Johansson L, Millqvist E, Nasic S, Bende M.** Relative frequencies of symptoms and risk factors among patients with chronic rhinosinusitis with nasal polyps using a case-control study. Acta Otolaryngol. 2018 Jan;138(1):46-49.

III. **Bohman A, Juodakis J, Oscarsson M, Bacelis J, Bende M, Torinsson-Naluai Å.** A family-based genome-wide association study of chronic rhinosinusitis with nasal polyps implicates several genes in the disease pathogenesis. PLoS One. 2017 Dec 18;12(12):e0185244.

IV. **Bohman A, Oscarsson M, Annor G, Bende M, Torinsson-Naluai Å.** A study of expression of genes implicated in a genome-wide association study on chronic rhinosinusitis with nasal polyps. (Manuscript)

SAHLGRENSKA AKADEMIN

GÖTEBORGS UNIVERSITET

Göteborg, 2019

Chronic Rhinosinusitis with Nasal Polyps

Symptoms, Heredity and Genetics

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Abstract

Chronic rhinosinusitis with nasal polyps (CRSwNP) is characterized by long-term inflammation of the paranasal sinuses combined with bilateral glassy protuberances from the middle meatus of the nasal cavity. This disease has an unknown cause, affects approximately 3% of the population and causes symptoms from the upper airways. This thesis addresses the heredity, symptoms and possible genetic factors of chronic rhinosinusitis with nasal polyps.

METHODS/RESULTS: **Paper I** investigates the prevalence of nasal polyps in a group of 410 first-degree relatives to patients with the same condition using nasal endoscopy and compares them to a control group of 1387 individuals from a previous study. 13.4% of the relatives had nasal polyps themselves, compared to 2.7% in the control group. The relative risk of the first-degree relatives having nasal polyps when compared to the control group was 4.9.

Paper II studies the symptoms and risk factors of 367 patients with CRSwNP and compares them to 1349 polyp-free controls. Symptoms and risk factors were gathered by a structured interview and compared in a multiple logistic regression model. Higher age, male sex, nasal blockage, impaired sense of smell, nasal secretions and asthma was more common among subjects with CRSwNP whereas smoking was less frequent.

Paper III is a family-based genome-wide association study that compares single nucleotide polymorphisms between 406 participants with CRSwNP and 376 of their polyp-free first-degree relatives. After association testing and post-GWAS analysis; *HLCS*, *HLA-DRA*, *BICD2*, *VSIR* and *SLC5A1* were the most significant. Of these five genes, only *HLA-DRA* had been implicated in CRSwNP previously.

Paper IV measures the expression levels of ten of the most significant genes from Paper III in peripheral blood from 76 individuals with CRSwNP and 45 of their polyp-free relatives and studies their eQTL patterns. *NDUFS5*, *CPEB3*, *HLCS* and *BICD2* were upregulated in cases. *HLCS*, *LYZ*, *PDGFD* and *TIAM1* showed differences in expression when examining participants with different genotypes.

CONCLUSIONS: First-degree relatives of patients with CRSwNP have an almost fivefold increased relative risk of having nasal polyps themselves when compared to controls. Nasal secretion, nasal blockage and decreased sense of smell are more common among subjects with CRSwNP than among controls. *HLCS*, *BICD2*, *VSIR* and *SLC5A1* are potential new genes of interest in CRSwNP. *HLA-DRA* is strengthened as a research target. *NDUFS5*, *CPEB3*, *HLCS* and *BICD2* are upregulated in peripheral blood samples from patients with CRSwNP when compared to controls. *HLCS*, *LYZ*, *PDGFD* and *TIAM1* displayed differences when comparing allelic expression.

Keywords: Nasal Polyps, Genetics, Signs and Symptoms, Genome-Wide Association Study, Gene Expression

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