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Rhinosinusitis without nasal polyps is associated with poorer health-related quality of life in COPD

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ABSTRACT

Rhinosinusitis without nasal polyps (RSsNP) is prevalent in COPD. Previous studies on its association with health-related quality of life (HRQoL) have limitations, and RSsNP is currently not recognized as a comorbidity. This study investigates HRQoL in COPD including a focus on RSsNP.

Generic HRQoL was assessed with the Short Form-36 (SF-36v2) questionnaire and compared between 90 COPD and 93 control subjects and in subgroups with and without RSsNP. The association between RSsNP and COPD versus not and generic HRQoL was assessed by multivariable linear regression with adjustments for age, education, and body mass index (BMI). Disease-specific HRQoL was assessed by Sinonasal outcome test-22 (SNOT-22), St. Georges Respiratory Questionnaire (SGRQ), and COPD Assessment Test (CAT) and compared between COPD with and without RSsNP, and their association to RSsNP was assessed by multivariable linear regression with adjustments for age, BMI, and FEV_1% predicted.

RSsNP was associated with poorer disease-specific HRQoL, with higher SNOT-22 total score (14.67 points; 95% CI, 7.06–22.28; $P < .001$) and psychological subscale score (3.24 points; 95% CI, 0.37–6.11; $P = .03$), SGRQ symptom score (13.08 points; 95% CI, 2.73–23.4; $P = .014$), and CAT score (4.41 points; 95% CI, 1.15–7.66; $P = .009$).

Generic HRQoL was poorer in COPD patients than in the control subjects. In addition to COPD, concomitant RSsNP was associated with poorer physical functioning, general health, vitality, and physical component summary.

RSsNP in COPD is associated with poorer disease-specific HRQoL that is clinically relevant and, as it is amenable for treatment, should be recognized as a comorbidity of COPD.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a disabling disease where patients with COPD experience respiratory symptoms and limited physical activity [1]. Moreover, cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety, and lung cancer are associated with and recognized as comorbidities in COPD [2]. In addition, chronic nasal symptoms are frequently observed in these patients [3–5].

Rhinosinusitis (RS) manifests as chronic nasal symptoms. The presence of two or more symptoms, one of which should be nasal obstruction and/or nasal discharge, and decreased sense of smell or facial pain/pressure and objective signs of disease on nasal endoscopy or CT scan,

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Abbreviations

BMI	Body Mass Index
BP	Bodily pain
CAT	COPD Assessment Test
COPD	Chronic Obstructive Pulmonary Disease
COPD - RSsNP	COPD without Rhinosinusitis sin Nasal Polyps
COPD + RSsNP	COPD with Rhinosinusitis sin Nasal Polyps
EPOS	European Position Paper on Rhinosinusitis and Nasal Polyps
GH	General health
HRQoL	Health-related quality of life
MCID	Minimal clinically important difference
MCS	Mental component summary
MH	Mental health
PCS	Physical component summary
PF	Physical functioning
RE	Role-emotional
RP	Role-physical
RS	Rhinosinusitis
RSsNP	Rhinosinusitis without (sin) nasal polyps
SF-36v2	Short Form-36 version 2.0 Health Survey
SGRQ	St. Georges Respiratory Questionnaire
SNOT-22	Sinonasal Outcome Test-22

are the diagnostic criteria of RS in the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2012) [6]. We have recently reported that the prevalence of RS without nasal polyps (RSsNP) is 51% and three times greater in a group of patients with COPD than in a control group comparable for age and sex [7]. In a review from 2015, RS was identified as the most prevalent underrecognized comorbidity of COPD [8] and is still not recognized as such. Not all comorbid diseases have clinical relevance, and focus should be on detecting those that are associated with important outcomes in COPD, such as Health-related quality of life (HRQoL) [2,9].

HRQoL is an individual's perception of the effect of health or chronic illness on the physical, psychological, and social domains of life [10–13], and both generic and disease-specific assessments should be conducted to display the burden of a disease [14,15]. In COPD, severity of the disease, comorbidities, chronic nasal symptoms, and RS are associated with impairment of HRQoL [1,9,16–22], and improvement of HRQoL is an important goal of clinical management [2,10]. However, previous studies on the association of RS with HRQoL in COPD have had limitations, such as non-standardized criteria for diagnosis of RS and COPD, lack of discrimination between RS with and without nasal polyps, assessment of HRQoL restricted to either generic or disease-specific instruments, and absence of a control group [19,21,23,24]. Only one study has adhered to the diagnostic criteria of EPOS and GOLD and that study explored if higher disease-specific HRQoL scores could predict chronic RS but did not assess generic HRQoL aspects related to RS [19]. Moreover, the clinical relevance of RSsNP as a comorbidity in patients with COPD needs attention.

The present study investigates HRQoL in COPD including a focus on RSsNP. Generic HRQoL was compared between patients with COPD and control subjects and in subgroup of participants with and without RSsNP. The association between RSsNP (yes/no) and COPD versus not and the outcome generic HRQoL was assessed, as well as the association between RSsNP and disease-specific HRQoL in the group of patients with COPD.

2. Material and methods

2.1. Participants and study design

The study sample of 90 patients with COPD and 93 control subjects was enrolled between February 2016 and December 2017 at St. Olavs hospital, Trondheim University Hospital, Norway in an observational cross-sectional study that has previously been published [7]. Briefly, patients with COPD were recruited from primary and secondary care settings and control subjects were recruited from the general population. For both groups, the inclusion criterion was age 40–80 years and the main exclusion criteria were previous sinonasal surgery, any systemic disease with a nasal manifestation, nasal tumour, asthma, symptoms of common cold within the previous two weeks, and the presence of nasal polyps on endoscopy. For the COPD group, additional exclusion criteria were exacerbation within the last 6 weeks and use of long-term oxygen therapy. All subjects provided informed consent, and approval by the National Ethical Committee of Norway was obtained (reference number 2015/2017). The study was conducted in accordance with the Helsinki Declaration.

2.2. Measurements

Self-administered questionnaires on age, sex, education, smoking habits, symptoms of allergy affecting the airways and, HRQoL were completed at the hospital under the guidance of a trained research nurse. Measurements of weight and height, skin prick test for sensitisation to birch, grass and mugwort pollen, cladosporium, house dust mite (Dermatophagoides pteronyssinus), and horse, dog and cat epithelia (Soluprick SQ, ALK-Abello, Horsholm, Denmark) [25], spirometry with reversibility test in accordance with European Respiratory Society standards [26], and a clinical interview with nasal endoscopy were performed on the same day. Educational level was divided into three categories: up to 9 years of schooling (primary), 12 years of schooling (secondary), and higher education (university). BMI was categorized according to World Health organization classification of nutritional status: Underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (>30 kg/m^2) [27].

2.3. Diagnosis

COPD diagnosis was based on the post-bronchodilator FEV_1/FVC ratio of <0.7 and a negative reversibility test to 0.4 mg salbutamol aerosol administered by spacer. The airflow limitation was classified in accordance with the GOLD guidelines [2] and reversibility testing was performed to exclude concomitant asthma. RSsNP diagnosis in both groups was made after inclusion, and in accordance with the EPOS 2012 criteria [6]. Allergic rhinitis was diagnosed based on symptoms of rhinoconjunctivitis on exposure to the specific allergen(s) with a positive skin prick test [28].

2.4. Health-related quality of life instruments

Generic HRQoL was measured with the Norwegian version of the SF-36v2 Health Survey Standard questionnaire (4-week recall) [15,29]. Scales for the domains of physical functioning (PF), role participation with physical health problems [role-physical (RP)], bodily pain (BP), general health, (GH) vitality (VT), social functioning (SF), role participation with emotional health problems [role-emotional (RE)], and mental health (MH) were derived from the 36 items. Component summary measures for physical health (PCS) and mental health (MCS) were computed from the PF, RP, BP and GH domains and VT, SF, RE and MH domains, respectively. The domain scales and summary measures were scored using QualityMetric Health Outcomes Scoring™ Software 5.0

[30] and reported as the 0–100 score for each domain scale and as the *T* score for each component summary measure. The latter score has been standardized against US population-based samples to have a mean of 50 ± 10 (SD) since no pan-European norms are available. For the domain scales and summary measures, higher scores indicate better HRQoL.

Disease-specific HRQoL for RS was measured with the SNOT-22 which is a 22-item questionnaire on sinonasal and non-sinonasal symptoms [31,32]. The items were rated from 0 to 5, with 5 indicating high severity. The total sum score is from 0 to 110, and a higher score implies a greater impact of these symptoms on HRQoL. Responses to items 13–15 ("difficulty falling asleep", "waking up at night", and "lack of good night's sleep"), and to items 17–22 ("fatigue", "reduced productivity", "reduced concentration", "frustrated/restless/irritable", "sad", and "embarrassed) were summated to 'Sleep' and 'Psychological' subscales, respectively [31,32]. The severity of sinonasal symptoms on HRQoL was determined by categorizing the SNOT-22 scores into mild (8−20), moderate (>20–50), and severe (>50) [33].

Disease-specific HRQoL for COPD was measured by Norwegian versions of the SGRQ [34,35] (one-month recall) and CAT questionnaires [36,37]. The SGRQ consists of 50 items and 76 weighted responses that assess the effects of respiratory symptoms, limitations due to breathlessness, and disturbances to psychological and social functioning in the 'Symptoms', 'Activity', and 'Impact' domains, respectively. Scores for the three domains and a total score were computed and range from 0 to 100, where higher scores indicate poorer HRQoL. The CAT questionnaire is a short, simple, reliable, and valid instrument of eight items: cough, phlegm, chest tightness, breathlessness going up hills/stairs, activity limitations at home, confidence leaving home, sleep, and energy [38,39]. Each item is scored from 0 to 5, and the total score ranges from 0 to 40, with higher scores indicating poorer HRQoL. The impact of COPD on HRQoL was determined by categorizing the CAT score into Low (1−10), Medium (11–20), High (21–30), and Very High Impact (31–40) [37].

2.4.1. Statistical analyses

Statistical analyses were performed using SPSS Statistics 25 (Statistical Packages for the Social Sciences, IBM Corporation, USA). The COPD and control groups were subdivided by RSsNP status. Categorical data are presented as frequencies and proportions and compared using the chi square test. Continuous data were normally distributed (tested by use of histograms for each group) and are presented as means and standard deviations (SD). Simple group and subgroup comparisons of continuous data were done using Student *t*-test. Multivariable linear regression analyses were performed to assess if COPD (vs not) and/or RSsNP (vs not) were associated with generic HRQoL in models adjusted for independent demographic (age and education) and health (BMI) variables. Further, multivariable analyses were used to explore if RSsNP (vs not) was associated with disease-specific HRQoL outcomes in patients with COPD and adjusted for age and health (BMI and FEV_1% predicted) variables. The Age and FEV_1% predicted covariates were modelled as continuous variables, and education and BMI as categorical variables. Sex was omitted from the regression analyses as this variable was not associated with either of the generic or disease-specific HRQoL outcomes in unadjusted analyses. Furthermore, smoking pack-years were assessed in unadjusted regression analyses for disease-specific HRQoL, but was not associated with the CAT and SGRQ and therefore omitted from further analyses. Allergic rhinitis was not included as a covariate in the analyses since only 5 COPD patients had allergic rhinitis. The assumptions of linear regression were verified using residual plots and tests of normality for the distribution of residuals. Statistical significance was set at a P value of .05.

3. Results

Characteristics of the COPD and control groups divided by RSsNP status are presented in Table 1. In the COPD group, Severe and Very Severe degree of airflow obstruction (GOLD 3–4) was present in 56.5% of patients with and 38.6% of patients without RSsNP.

3.1. RSsNP and generic HRQoL

The summary scores for physical (PCS) and mental health (MCS), and

Table 1
Subject characteristics.

Characteristics		COPD + RSsNP (n = 46)		COPD -RSsNP (n = 44)		p-value	Control + RSsNP (n = 15)		Control -RSsNP (n = 78)		p-value
Age, y	mean ± SD	66.2	±8.7	66.1	±8.8	1.0	67.3	7.0	63	±8.9	0.08
Male	n (%)	27	(58.7)	22	(50)	0.4	8	(53.3)	43	(55.1)	0.9
Education											
Primary (≤9 y)	n (%)	15	(32.6)	16	(36.4)		0	(0)	6	(7.7)	
Secondary (10–12 y)	n (%)	19	(41.3)	17	(38.6)		5	(33.3)	22	(28.2)	
University (≥13 y)	n (%)	11	(23.9)	11	(25)		10	(66.7)	50	(64.1)	
Smoking Status											
Current	n (%)	11	(23.9)	6	(13.6)		2	(13.3)	5	(6.4)	
Former	n (%)	32	(69.6)	36	(81.8)		9	(60)	38	(48.7)	
Never	n (%)	3	(6.5)	2	(4.6)		4	(26.7)	35	(44.9)	
Pack-years smoked[a]	mean ± SD	26.5	±22.2	30.9	±19.5	0.3	11.5	±15.7	5.6	±9.4	0.2
BMI, kg/m^2	mean ± SD	26.8	±5.5	27.3	±5.3	0.7	27.6	±2.5	27.3	±5.0	0.8
Underweight (<18.5)	n (%)	0	(0)	0	(0)		0	(0)	2	(2.6)	
Normal (18.5–24.9)	n (%)	19	(41.3)	16	(36.4)		2	(13.3)	21	(26.9)	
Overweight (25–29.9)	n (%)	18	(39.1)	18	(40.9)		11	(73.3)	36	(46.2)	
Obese (≥30)	n (%)	9	(19.6)	10	(22.7)		2	(13.3)	19	(24.4)	
Allergic Rhinitis	n (%)	5	(10.9)	0	(0)		3	(20)	11	(14.1)	
Pulmonary function[b]											
FEV_1 % predicted	mean ± SD	49.4	±18.3	57.1	±18.5	0.052	94.7	±12.2	94.9	±12.3	1.0
FEV_1/FVC ratio	mean ± SD	0.52	±0.13	0.55	±0.13	0.2	0.79	±0.05	0.78	±0.05	0.5
Airflow obstruction											
GOLD 1	n (%)	2	(4.3)	5	(11.4)						
GOLD 2	n (%)	18	(39.1)	22	(50)						
GOLD 3	n (%)	19	(41.3)	14	(31.8)						
GOLD 4	n (%)	7	(15.2)	3	(6.8)						

COPD = Chronic Obstructive Pulmonary Disease; + RSsNP = with Rhinosinusitis without Nasal Polyps; - RSsNP = without Rhinosinusitis without Nasal Polyps; BMI = Body mass index; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

[a] Missing data in four control subjects and three patients with COPD.

[b] Post-bronchodilator measurements, pre-bronchodilator values in two control subjects and one patient with COPD.

the 0–100 scale scores of the eight domains in SF-36v2 were significantly lower in COPD than in the control group (Fig. 1). In subgroup analyses, PCS, MCS, and domain scores were not significantly different between subjects with and without RSsNP in the COPD group (Fig. 2, Table 2). Of these scores, GH was significantly lower in subjects with than without RSsNP in the control group. In multivariable regression analyses, RSsNP was associated with poorer PCS (Table 3a), and PF, GH, and VT domains in SF-36v2 when adjusting for COPD and other socio-demographic and health variables (Table 3b).

3.2. RSsNP and disease-specific HRQoL in COPD

The total SNOT-22 and Psychological subscale scores were significantly greater in COPD with RSsNP compared to those without RSsNP, with mean ± SD values of 36.8 ± 18.1 vs 22.6 ± 16.8 and 9.5 ± 6.9 vs 6.5 ± 6.4, respectively ($P < .05$) (Fig. 3A). Among COPD patients with and without RSsNP, 20% (9/46) and 30% (13/44) had mild sinonasal disease, 57% (26/46) and 39% (17/44) had moderate disease, and 24% (11/46) and 7% (3/44) had severe disease, respectively. In adjusted multivariable regression analyses, RSsNP was associated with higher total SNOT-22 and Psychological subscale scores (Table 4).

The total score and scores for the Symptom and Activity domains in the SGRQ were significantly greater in COPD patients with RSsNP than without RSsNP (Fig. 3B), with respective mean ± SD values of 43.3 ± 17.6 vs 34.0 ± 19.2, 50.6 ± 23.9 vs 34.5 ± 26.7, and 57.1 ± 20.3 vs 46.8 ± 23.6 ($P < .05$). There was no statistically significant difference in the Impact domain score [mean ± SD 32.8 ± 17.7 vs 26.0 ± 19.2 ($P = .08$)]. In adjusted multivariable regression analyses, RSsNP was significantly associated with a higher SGRQ Symptom domain score, which was on average 13.1 points higher than in patients without RSsNP (Table 4).

The total CAT score was significantly greater in COPD with RSsNP than without RSsNP (mean ± SD of 18.8 ± 7.9 vs 13.5 ± 8.0) ($P < .05$) (Fig. 3C). Patients with RSsNP were four times more likely to have CAT scores indicating High or Very High impact on HRQoL compared to patients without RSsNP (41% vs 9%, $P < .001$) (Fig. 3D). In adjusted multivariable regression analyses, concomitant RSsNP was significantly associated with a higher total CAT score, which was on average 4.4 points higher than in patients without RSsNP.

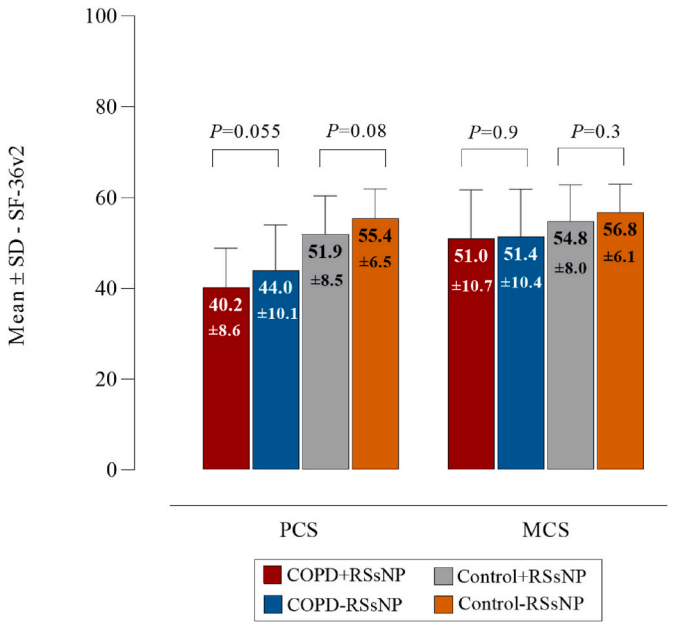

Fig. 2. Generic HRQoL Component summary scores (PCS and MCS) by RSsNP status in COPD and control subjects.

4. Discussion

The primary finding of this study is that concomitant RSsNP in patients with COPD is associated with poorer disease-specific HRQoL.

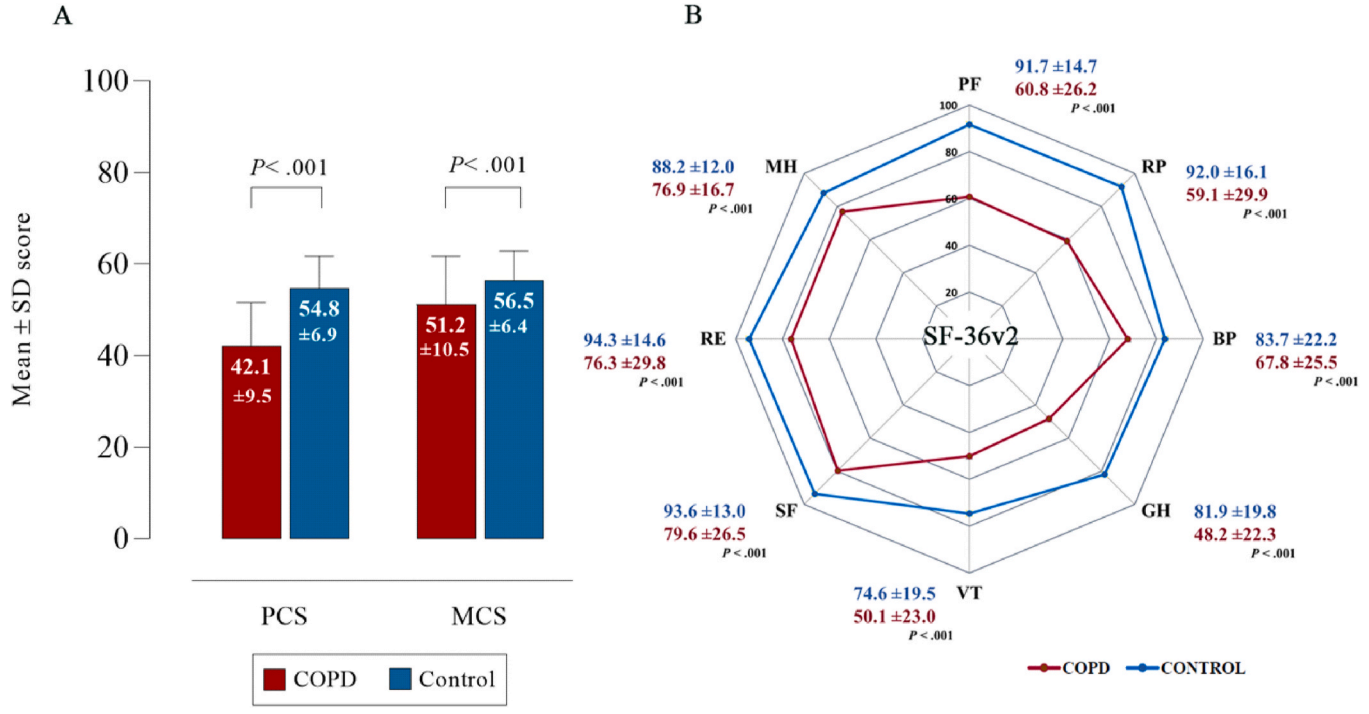

Fig. 1. Generic HRQoL in patients with COPD and control subjects assessed with SF-36v2.
A) Component summary scores; B) Health domain scale scores.
Data presented as mean ± SD. PCS = physical component summary; MCS = mental component summary; PF = physical functioning; RP = role-physical; BP = bodily pain; GH = general health; VT = vitality; SF = social functioning; RE = role-emotional; MH = mental health.

Table 2
Generic HRQoL 0–100 scale scores in patients with COPD and control subjects with and without RSsNP.

SF-36v2 health domains	COPD - RSsNP (n = 44)		COPD +RSsNP (n = 46)		p-value	Control - RSsNP (n = 78)		Control + RSsNP (n = 15)		p-value
Physical functioning (PF)	64.8	±26.8	57.1	±25.4	0.2	93.0	±10.9	84.7	±26.4	0.2
Role-physical (RP)	61.4	±31.2	56.9	±28.8	0.5	93.0	±15.0	87.1	±20.8	0.2
Bodily pain (BP)	72.6	±26.5	63.2	±24.0	0.08	84.6	±21.3	79.2	±26.8	0.4
General health (GH)	52.4	±22.3	44.1	±21.7	0.08	83.9	±18.6	71.3	±23.0	0.02
Vitality (VT)	52.6	±22.6	47.8	±23.5	0.3	75.9	±19.0	67.9	±21.5	0.2
Social functioning (SF)	82.7	±26.9	76.6	±26.0	0.3	94.2	±12.0	90.0	±17.2	0.3
Role-emotional (RE)	78.0	±31.1	74.6	±28.7	0.6	95.1	±12.7	90.0	±22.3	0.4
Mental health (MH)	76.7	±16.7	77.2	±16.9	0.9	88.9	±11.5	84.7	±14.2	0.2

Data presented as mean ± SD. HRQoL = Health-related Quality of life; SF-36v2 = Short Form-36version2; See Table 1 legend for expansion of abbreviations.

Table 3a
Adjusted associations between RSsNP and Generic HRQoL (SF-36v2) component summary scores in patients with COPD and control subjects.

Variables *	Physical Component Summary (PCS)	Mental Component Summary (MCS)
	β coefficient ∞ 95% CI	β coefficient ∞ 95% CI
COPD (Control)	−11.28 ** −14.06 to −8.49	−3.98 ** −6.96 to −1.0
RSsNP	−3.53 ** −6.19 to −0.86	−1.51 −4.36 to 1.34
Adjusted R^2	0.42	0.12

RSsNP is associated with more psychological issues, higher COPD symptom burden, and poorer overall COPD-related HRQoL, after adjustment for % predicted FEV_1. For generic HRQoL, RSsNP is associated with lower scores for the physical component summary and the physical functioning, general health, and vitality domains, after adjustment for COPD. The secondary finding is that patients with COPD without concomitant asthma have poorer generic HRQoL, with lower summary and domain scores of the SF-36v2, in comparison to control subjects.

The present study shows that RSsNP was highly associated with the overall disease-specific HRQoL measured with the CAT questionnaire in adjusted multivariable regression analyses. This association has been reported by two other studies [19,21], and is an addition to previous findings as patients with nasal polyps, which is a different clinical phenotype of RS, were excluded and multivariable statistical analyses to adjust for covariates of possible importance, were performed in the present study.

Furthermore, patients with COPD and concomitant RSsNP were four times more likely to have CAT scores indicating High or Very High impact on HRQoL compared to those without RSsNP. The clinical relevance of a High impact on HRQoL, according to the COPD ladder of severity, translates into “stop doing most of what they want to do”, “exercise is not safe and everything seems too much of an effort”, and “no good days in the week” [36]. This suggests that having RSsNP substantially adds to the activity limitation experienced by patients with COPD. In contrast, there was no significant association between RSsNP and the Activity domain of the SGRQ in the adjusted multivariable regression analyses. A possible explanation could be that the Activity domain measures limitation due to breathlessness whilst the CAT has a question solely on activity limitation at home. The Symptom domain in the SGRQ was significantly associated with RSsNP and patients with COPD experience symptoms that progressively compromise their physical capacity. We also found that RSsNP was significantly associated with poorer physical functioning after adjusting for COPD in the SF-36v2. Physical inactivity in daily life is increasingly recognized as an important outcome in COPD and is associated with mortality and the development of comorbidities [40,41]. These results indicate that patients with COPD and concomitant RSsNP have added activity limitation and an increased symptom burden.

In the present study, concomitant RSsNP in patients with COPD was associated with sadness, embarrassment, frustration/irritability, fatigue, and reduced concentration and productivity (SNOT-Psychological). Conversely, we did not find that the increased sinonasal burden of RSsNP affected sleep quality in these patients (SNOT-Sleep). It seems that the sleep disturbance that is known to be present in patients with COPD [22,42], was not exacerbated by the symptoms of RSsNP.

The upper limit of the SNOT-22 score in persons with no sinonasal disease has been reported to be 7 [43,44]. Most of the COPD patients in our study (88%) had a SNOT score above this upper limit, which agrees with the SNOT scores presented in the study by Arndal et al. [19]. Patients with COPD without RSsNP had a mean SNOT-22 score of 22.6 (Fig. 3A). Moreover, based on criteria suggested by Toma et al. for determining the severity of sinonasal disease [33], 75% (33/44) of our COPD patients without RSsNP had a mean SNOT score equal or higher than 8, and 45% (20/44) classified as moderate/severe. This suggests

Table 3b
Adjusted associations between RSsNP and Generic HRQoL (SF-36v2) health domain scale scores in patients with COPD and control subjects.

Variables [a]	Physical Functioning (PF)	Role-Physical (RP)	Bodily Pain (BP)	General Health (GH)	Vitality (VT)	Social Functioning (SF)	Role-Emotional (RE)	Mental Health (MH)
	β coefficient [b] 95% CI	β coefficient [b] 95% CI	β coefficient [b] 95% CI	β coefficient [b] 95% CI	β coefficient [b] 95% CI	β coefficient [b] 95% CI	β coefficient [b] 95% CI	β coefficient [b] 95% CI
COPD (Control)	−24.64 ** −31.56 to −17.72	−28.90 ** −37.03 to −20.77	−14.26 ** −22.50 to −6.02	−30.54 ** −37.81 to −23.26	−20.71 ** −28.01 to −13.40	−12.08 ** −19.33 to −4.84	−11.61 ** −19.50 to −3.73	−9.81 ** −14.86 to −4.76
RSsNP	−7.56§ −14.18 to −0.95	−5.09 −12.86 to 2.68	−7.45 −15.31 to −0.44	−10.20 ** −17.15 to −3.24	−7.08§ −14.06 to −0.09	−6.17 −13.10 to 0.76	−4.76 −12.29 to 2.78	−1.77 −6.60 to 3.06
Adjusted R^2	0.43	0.36	0.13	0.41	0.28	0.11	0.19	0.14

[a] Continuous variables: age. Categorical variables: diagnosis (COPD = 1, control = 0), RSsNP (yes = 1, no = 0), education (secondary vs primary and university vs primary), BMI (overweight vs normal weight and obese vs normal weight).
[b] Regression coefficients are adjusted for the variables listed in the table, as well as age, education, and BMI.§p < .05, **p < .01.

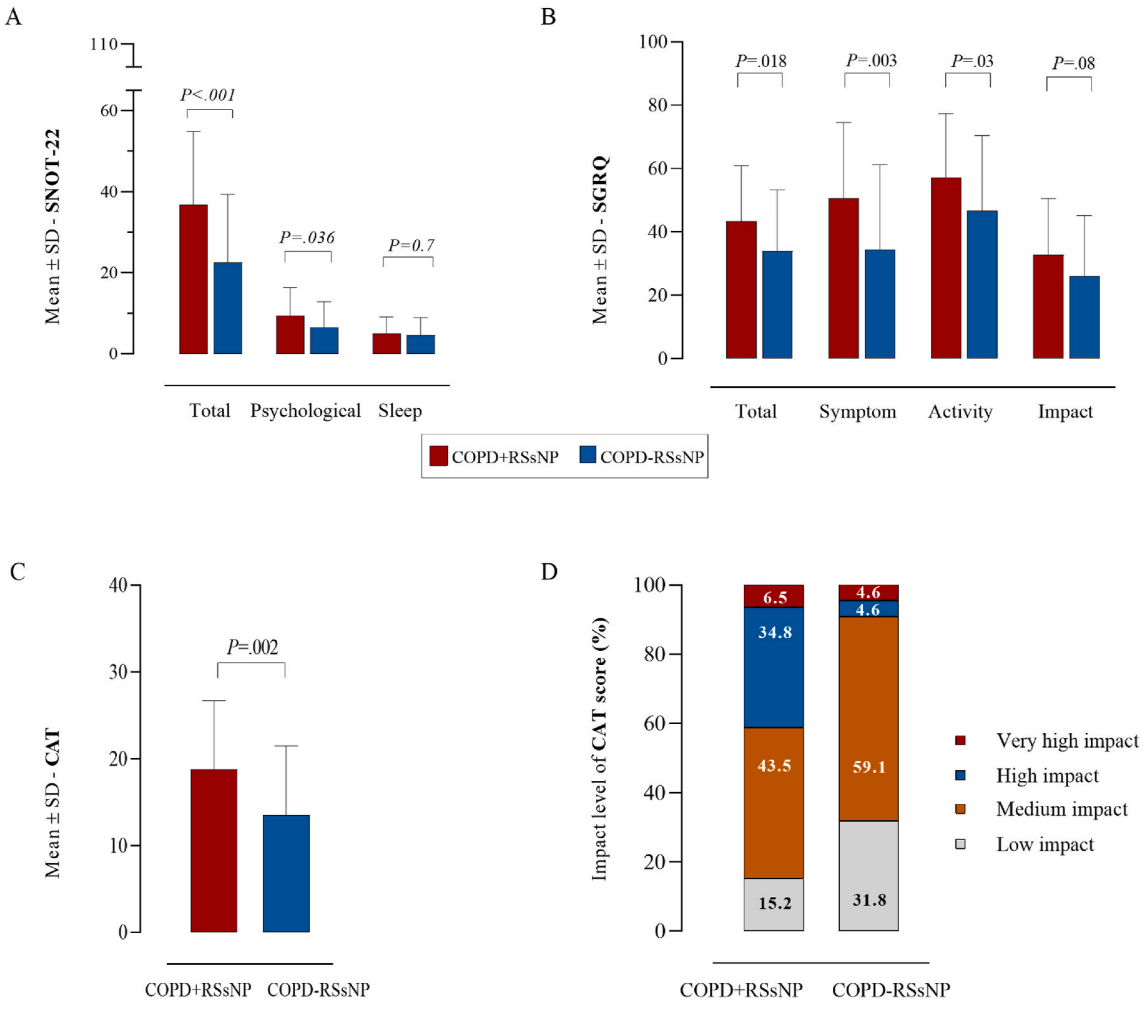

Fig. 3. Disease-specific HRQoL by RSsNP status in patients with COPD.
A) SNOT-22 – Sinonasal outcome test-22, total and subscale scores. B) SGRQ – St. Georges Respiratory Questionnaire, total and domain scores. C) CAT – COPD Assessment Test, total score. D) Impact level of CAT score on HRQoL.

Table 4
Adjusted associations between RSsNP and disease-specific HRQoL outcomes in patients with COPD.

	SNOT-22			SGRQ				CAT
	Total score	Psychological issues	Sleep Function	Total score	Symptom score	Activity score	Impact score	Total score
Variables [a]	β coefficient[b] 95% CI	β coefficient[b] 95% CI	β coefficient[b] 95% CI	β coefficient[b] 95% CI	β coefficient[b] 95% CI	β coefficient[b] 95% CI	β coefficient[b] 95% CI	β coefficient[b] 95% CI
FEV_1% predicted	0.06 −0.15 to 0.27	0.02 −0.67 to 0.10	0.01 −0.04 to 0.06	−0.44 ** −0.64 to −0.25	−0.44 ** −0.73 to −0.15	−0.59 ** −0.79 to −0.38	−0.36 ** −0.57 to −0.15	−0.13 ** −0.22 to −0.04
RSsNP	14.67 ** 7.06 to 22.28	3.24§ 0.37 to 6.11	0.45 −1.41 to 2.32	6.33 −0.60 to 13.26	13.08§ 2.73 to 23.44	6.41 −0.92 to 13.74	4.34 −3.16 to 11.83	4.41 ** 1.15 to 7.66
Adjusted R^2	0.11	0.04	−0.05	0.27	0.17	0.42	0.13	0.18

[a] Continuous variables: age, FEV_1% predicted. Categorical variables: RSsNP (yes = 1, no = 0), BMI (overweight vs normal weight and obese vs normal weight).
[b] Regression coefficients are adjusted for the variables listed in the table, as well as age and BMI.§p < .05, **p < .01.

that COPD patients without RSsNP have a sinonasal symptom burden that is greater than that of persons with no sinonasal disease.

We found RSsNP to be associated with poorer generic HRQoL in our sample when controlling for COPD. However, van Manen et al. [45] who investigated how comorbidity was associated with generic HRQoL found that COPD, rather than comorbidity had a greater influence on PCS, PF, GH, and VT domains. Even so, the definition of comorbidity used in that study was at least one positive self-reported answer to a questionnaire of 23 diseases and symptoms with a prevalence in excess 2% in the Dutch population. Further, participants in the present study were not specifically asked about chronic conditions or symptoms of comorbid diseases, and concomitant RSsNP was a clinical diagnosis based on the EPOS criteria.

Our secondary finding of poorer generic HRQoL in patients with COPD, with lower summary scores and domain scores of the SF-36v2 in univariable and multivariable linear regression analyses are consistent with previous research [45–47]. Similar findings for the SF-36 were reported in Norwegian patients with COPD in the study by Bentsen et al. [48] on comparison of these patients with controls without chronic conditions and adjusted for age and sex. The use of the SF-36v2 and

inclusion of a comparable control group in the present study corroborates and extends the findings of those prior studies.

Improvement of HRQoL is an important management goal in COPD [2]. In the present study, the total mean SGRQ score is 6.3 points, CAT score is 4.4 points, and total SNOT-22 score is 14.7 points greater in patients with than without concomitant RSsNP. These scores exceed the minimally clinically important difference of 4, 2 and 12 points, respectively [35,49,50], that is required to show efficacy in an intervention study and raises the intriguing question of whether diagnosis and medical treatment of RSsNP will improve the disease-specific HRQoL of this subgroup of COPD patients.

The main strengths of this study are the inclusion of control subjects from a comparable population with the same geographic and demographic variation and during the same time span for assessment of generic HRQoL, almost equal distribution of the sexes in the COPD group, and the use of standardized criteria for COPD and RSsNP. The latter ensures that the results are not attributable to asthma and nasal polyps. Further, the present study assessed generic HRQoL with the SF-36v2 questionnaire. Knowledge of generic HRQoL in COPD has mainly been based on the SF-36 questionnaire. The main differences between the two versions are improvement in instructions, item wording and layout, and changes in choice of response from dichotomous to five levels of response [15]. It is thus reassuring that the findings of generic HRQoL in the present study are comparable with those of previous studies.

Some limitations should also be addressed. Firstly, we did not examine comorbidities that potentially could contribute to poorer HRQoL in patients with COPD. However, van Manen et al. [45] investigated the influence of comorbidity on HRQoL in COPD and found that the prevalence and number of chronic diseases were not different between patients with COPD and controls. It is therefore likely to assume that accounting for comorbidities would not have affected the results. Secondly, the cross-sectional study design precludes conclusions on direction of influence of the associations between RSsNP and HRQoL in COPD. Further, the diagnosis of RSsNP conducted post inclusion resulted in uneven subgroup sample sizes with little statistical power for multivariable statistical analyses for COPD and controls separately. Finally, the generalizability of our results to other populations may be limited, as the participants in the present study were of white Caucasian descent and COPD patients without concomitant asthma. On the other hand, this also makes our results less dependent on the influence of geographic and demographic variation, as well as external environmental factors such as social support and cultural expectations.

5. Conclusion

RSsNP is associated with poorer disease-specific HRQoL in COPD. We found that RSsNP in COPD has clinical relevance and support previous studies that have suggested that RSsNP should be recognized as a comorbidity in patients with COPD.

The present study provides additional evidence that the united airway disease concept may also be applicable for COPD and RS. It is thus important to diagnose and manage RSsNP in COPD.

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CRediT authorship contribution statement

Marte Rystad Øie: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Malcolm Sue-Chu:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision. **Anne-Sofie Helvik:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision. **Sverre Karmhus Steinsvåg:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision. **Silje Steinsbekk:** Conceptualization, Writing – original draft, Writing – review & editing. **Wenche Moe Thorstensen:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Funding acquisition, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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