Rekrytering av aldrig-rökare med kroniskt obstruktiv lungsjukdom från den populationsbaserade Swedish CArdioPulmonary bioImage Study (SCAPIS)

Pernilla Sönnerfors[1], Petra Jacobson[2], Anders Andersson[3], Leif Bjermer[4], Anders Blomberg[5], Heléne Blomqvist[6], Jonas Erjefeldt[7], Christer Janson[8], Andrei Malinovschi[9], Lennart Persson[2], Ellen Tufvesson[4], Åsa Wheelock[6], Magnus Sköld[6]

[1] Respiratory Medicine Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden. Medical Unit Occupational therapy and Physiotherapy, Women´s Health and Allied Health Professionals Theme, Karolinska University Hospital, Stockholm, Sweden, [2] Department of Respiratory Medicine in Linköping, Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden., [3] COPD Center, Department of Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, and COPD Center Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [4] Department of Clinical Sciences, Respiratory medicine, allergology and palliative medicine, Lund University, Lund, Sweden, [5] Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden, [6] Respiratory Medicine Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden. Department of Respiratory Medicine and Allergy, Karolinska University Hospital, Stockholm, Sweden, [7] Unit of Airway inflammation, Department of Experimental Medicine Sciences, Lund University, Lund, Sweden, [8] Department of Medical Sciences, Respiratory, Allergy and Sleep Research, Uppsala University, Uppsala, Sweden, [9] Department of Medical Sciences, Clinical Physiology, Uppsala University, Uppsala, Sweden

Bakgrund: En betydande del av personer med kroniskt obstruktiv lungsjukdom (KOL) har aldrig rökt och denna grupp är bristfälligt studerad. Syftet med studien var att beskriva rekryteringsprocessen för en subgrupp av aldrig-rökare med KOL från en befintlig populationsbaserad studie (n=30,154).

Material och metod: Vi inkluderade aldrig-rökare med KOL som var 50-75 år från sex svenska universitetssjukhus enligt följande kriterier 1) forcerad expiratorisk volym på 1 sekund/forcerad vitalkapacitet (FEV1/FVC) < 0,70 efter luftrörsvidgande läkemedel och 2) FEV1 50-100 % av förväntat värde och 3) aldrig-rökare (självrapporterat). Totalt identifierades 862 aldrig-rökare med KOL i SCAPIS kohorten, varav 652 kunde nås och var positiva till en första screening via telefon. Efter den första kontakten exkluderades 128 (20 %) (tackade nej eller hade rökt). För att säkerställa att endast deltagare med obstruktivitet inkluderades användes även det nedre normalgränsvärdet (LLN) FEV1/FVC < LLN (z-score < -1,64) enligt Global Lung Initiative (GLI).

Resultat: Data om luftvägssymtom, hälsotillstånd och sjukdomshistoria samlades in från totalt 492 individer, eftersom 32 deltagare blev exkluderade efter en andra datagranskning innan det första besöket (tackade nej eller hade rökt). På grund av att lungfunktionskriterierna inte uppfylldes vid en andra spirometri exkluderades ytterligare 334 (68 %). Orsakerna var FEV1/FVC ≥ 0,7 (49 %), FEV1>100 % av förväntat värde (26 %) eller z-score ≥ -1,64 (24 %). Slutligen inkluderades 154 aldrig-rökare med KOL, 56 (36 %) kvinnor, (medel) ålder 60 år, FEV1 84 % av förväntat värde, FEV1/FVC: 0,6, z-score: -2,2, syremättnad: 97 %, BMI: 26,8 kg/m2.

Slutsats: Utmaningarna vid en rekryteringsprocess av aldrig-rökare med KOL visades och innefattade betydelsen av korrekt utförd spirometriundersökning och strikta inklusionskriterier. Våra resultat belyser vikten av upprepade undersökningar för förbättrad precision vid diagnostisering av KOL.

Associations of comorbid conditions with persistent breathlessness and different dimensions of dyspnea in COPD – a cohort study

Gabriella Eliason[1], Magnus Ekström[2], Scott Montgomery[3,4,5], Maaike Giezeman[6], Mikael Hasselgren[6,7], Christer Jansson[8], Marta A Kisiel[9], Karin Lisspers[10], Anna Nager[11], Hanna Sandelowsky[3,11,12], Björn Ställberg[10], Josefin Sundh[1]

[1] Department of Respiratory Medicine, Faculty of Medicine and Health, Örebro University, Örebro, Sweden., [2] Lund University, Faculty of Medicine, Department of Clinical Sciences Lund, Respiratory Medicine, Allergology and Palliative Medicine, Lund, Sweden. , [3] Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [4] Clinical Epidemiology and Biostatistics, School of Medical Sciences, Faculty of Medicine and Health, Örebro University, Örebro, Sweden, [5] Department of Epidemiology and Public Health, University College London, London, UK, [6] School of Medical Sciences, Faculty of Medicine and Health, Örebro University, Örebro, Sweden., [7] Centre for Clinical Research and Education, Karlstad, Sweden, [8] Department of Medical Sciences, Respiratory, Allergy and Sleep Research, Uppsala University, Uppsala, Sweden, [9] Department of Medical Sciences, Occupational and Environmental Medicine, Uppsala University, Uppsala, Sweden, [10] Department of Public Health and Caring Sciences, Family Medicine and Preventive Medicine, Uppsala University, Uppsala, Sweden, [11] NVS, Section for Family Medicine and Primary Care, Karolinska Institutet, Stockholm, Sweden, [12] Academic Primary Care Centre, Region Stockholm, Sweden

Background: Comorbid conditions and breathlessness, the multidimensional experience of breathing discomfort, associate with poor outcomes in chronic obstructive pulmonary disease (COPD). We aimed to explore the associations of comorbid heart disease and depression/anxiety with different dimensions of breathlessness in patients with COPD.

Methods: Cohort study design including 522 patients from the PRAXIS-study in mid-Sweden. In 2014, baseline data were collected from questionnaires on patient characteristics and by medical record reviews for spirometry and comorbid conditions. In 2022, data on breathlessness from the modified Medical Research Council (mMRC) breathlessness scale and Dyspnea-12 (D-12) scores were obtained from a follow-up questionnaire. Outcomes were mMRC≥2 and increased D-12 total-, physical- and affective scores both as continuous variables and as a rating > the minimal important difference. Associations of heart disease and depression/anxiety with each outcome were analyzed using multivariable linear and logistic regression adjusted for sex, age, body mass index, smoking status, exacerbations and level of airflow limitation at baseline.

Results: In total, 522 patients (57% women) were included in the study, of whom 17% had comorbid heart disease, 19% had depression/anxiety and another 4% had both heart disease and depression/anxiety. MMRC > 2 was present in 59%, and increased binarized Dyspnea-12 total, physical and affective domain scores in 69%, 74% and 50%, respectively. Heart disease was independently associated with D-12 total (regression coefficient [95% CI] 0.22 [0.003-0.43], p=0.033) and physical domain (0.21 [0.03-0.2)], p=0.021) scores. Depression was independently associated with binarized D-12 total score (odds ratio 1.91; [95% CI] 1.14-3.22).

Conclusion: Comorbid heart disease and depression/anxiety are associated with increased risk of breathlessness in patients with COPD, and the D -12 instrument seems to be more sensitive than the traditional mMRC scale in detecting breathlessness in patients with COPD and comorbid conditions.

Clinical phenotypes predict exacerbations of COPD: the TIE cohort study

Jens Ellingsen[1], Christer Janson[1], Kristina Bröms[2], Amir Farkhooy[3], Maria Hårdstedt[4], Marieann Högman[1], Karin Lisspers[2], Andreas Palm[1], Björn Ställberg[2], Andrei Malinovschi[3]

[1] Department of Medical Sciences, Respiratory, Allergy & Sleep Research, Uppsala University - Uppsala (Sweden), [2] Department of Public Health & Caring Sciences, Family Medicine & Preventive Medicine, Uppsala University - Uppsala (Sweden), [3] Department of Medical Sciences, Clinical Physiology, Uppsala University - Uppsala (Sweden), [4] Center for Clinical Research Dalarna - Uppsala University - Falun (Sweden)

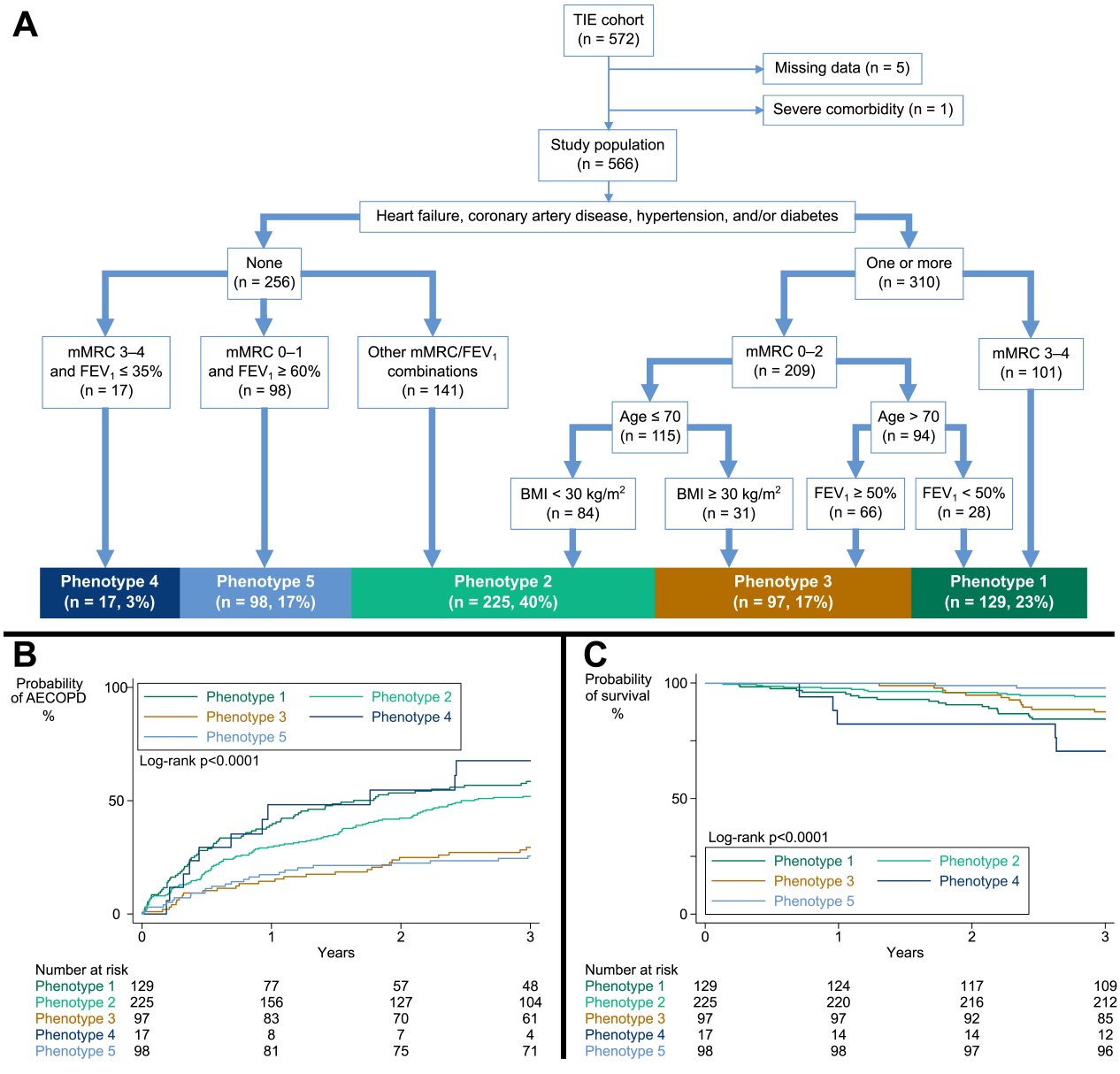
Background: In 2017, Burgel and colleagues developed an algorithm to identify clinical phenotypes that predict mortality in COPD. Our study aimed to 1) investigate whether the clinical phenotypes can predict acute exacerbations of COPD (AECOPDs) and 2) validate their ability to predict mortality.

Methods: The Tools Identifying Exacerbations (TIE) cohort study recruited participants with spirometry-verified COPD from primary and secondary care in three Swedish regions. Participants were allocated to phenotypes 1–5 using the previously developed algorithm containing comorbidities (heart failure, coronary artery disease, hypertension and/or diabetes), dyspnoea, age, forced expiratory volume in one second (FEV1), and body mass index (BMI) (Figure, panel A). AECOPDs and deaths during the three-year follow-up were collected from medical records and analysed with Kaplan-Meier (KM) curves and Cox proportional hazards regressions. Harrel's C-index (HCi) was used to assess the Cox models' discriminative ability.

Results: Among the 566 participants, 59% were female, and the mean±SD FEV1 was 57±18% predicted. Figure, panel B, shows the KM curves of AECOPD probability. The hazard ratios (HRs) [95% CI] for time to AECOPD were 3.04 [1.93–4.79], 2.38 [1.54–3.66], and 3.52 [1.73–7.15] in phenotypes 1, 2, and 4 compared with 5 (HCi = 0.61). As a comparator, HCi for FEV1 severity grades 1–4 was 0.62.

Figure, panel C, shows the KM curves of survival probability. The HRs [95% CI] for mortality were 8.24 [1.93–35.3], 6.26 [1.40–28.0], and 16.7 [3.25–86.3] in phenotypes 1, 3, and 4 compared with 5 (HCi = 0.68). HCi for FEV1 severity grades 1–4 was 0.61.

Conclusion: Clinical COPD phenotypes based on comorbidities, dyspnoea, age, FEV1, and BMI predict AECOPDs but do not perform better than FEV1 alone. However, the phenotypes predict mortality better than FEV1.



Cardiovascular prevalence, mortality and associations with treatment in oxygen-dependent COPD - a national cohort study

Josefin Sundh[1], Yet Khor[2], Zainab Ahmadi[3], Mirjam Ljunggren[4], Ludger Grote[5], Andreas Palm[4], Magnus Ekström[3]

[1] Örebro University, Örebro, Sweden, [2] Monash University, Melbourne, Australia , [3] Lund University, Lund, Sweden, [4] Uppsala University, Uppsala, Sweden , [5] Gothenburg University, Gothenburg, Sweden

Background
Chronic obstructive pulmonary disease (COPD) is associated with increased risk for cardiovascular disease (CVD). We aimed to explore temporal changes in CVD prevalence and cardiovascular (CV) mortality and associations with treatment in patients with COPD and long-term oxygen therapy (LTOT).

Methods
Population-based DISCOVERY cohort study using data from 1987 to 2022 from the Swedish National Registry for Respiratory Failure and the National Patient Registry. Annual prevalence of CVD (ischemic heart disease, heart failure, atrial fibrillation/flutter, cerebral infarctions/ hemorrhages) at start of LTOT and all cause-, and CV mortality rates per year were calculated. Associations of beta-blockers, ACE/AI-inhibitors, statins and inhaled corticosteroids (ICS) with CV mortality and new acute CV events (myocardial infarctions or cerebral infarctions/hemorrhages) were analysed using Cox regression, adjusting for sex, age, PaO2 on air, body mass index, performance status, forced expiratory volume in one second, CVD and exacerbation frequency at LTOT start.

Results
During the study period, 18,733 patients (58% women, mean age+SD 74+8 years) started LTOT, and of these 17,066 died. The CVD prevalence at LTOT start changed from 21% in 1989 to 51% in 2022. Mortality rate decreased from 38 to 34 % (all-cause) and from 5.4% to 4.6% (CV). The proportion of CV deaths was unchanged at 14%. ICS treatment was independently associated with lower risk for CV mortality (HR [95%CI] 0.75 [0.66-0.86]) and for new acute CV events (0.78 [0.70-0.87]).

Conclusions
CVD prevalence but not CV mortality has increased in oxygen-dependent COPD. ICS may be of benefit to prevent CV events.

Prevalence of microspirometry-defined chronic obstructive pulmonary disease in two European cohorts of patients with significant smoking history hospitalised for acute myocardial infarction

Josefin Sundh[1], William AE Parker[2], Jonas Oldgren[3], Kyriakos V Konstantinidis[4], Johan Lindbäck[3], Christer Janson[3], Pontus Andell[5], Anna Björkenheim[1], Nadir Elamin[2], Hannah McMellon[2], Mehul Patel[4], JadEl Khoury[4], Raulin Surujbally[4], Robert F Storey[2], Stefan James[3]
[1] Örebro University, Örebro, Sweden, [2] University of Sheffield, Sheffield, UK, [3] Uppsala University, Uppsala, Sweden, [4] AstraZeneca, Cambridge, UK, [5] Karolinska Institutet, Stockholm, Sweden

Background
Smoking is a major risk factor for both chronic obstructive pulmonary disease (COPD) and myocardial infarction (MI). Systemic inflammation contributes to both diseases and has been suggested as a potential target for intervention. We sought to obtain an accurate estimate of COPD burden among patients with MI and characterise the population.

Methods
Two consecutive cohorts of patients hospitalised for MI with a smoking history of >10 pack-years were recruited in Sweden and the United Kingdom (UK). Microspirometry was performed using the Vitalograph COPD-6 device and symptom burden assessed using the COPD Assessment Test (CAT). Baseline characteristics were recorded, including inhaled treatments, blood eosinophil count and past medical history. The primary outcome was the prevalence of a preliminary diagnosis of clinically significant COPD, defined as a ratio of forced expiratory volume in 1 and 6 seconds (FEV1/FEV6) <0.7 and with FEV1 <80% of predicted value.

Results
The prevalence of significant COPD was 39/216 (18%) in the UK cohort, 52/302 (17%) in the Swedish cohort and 91/518 (18%) in the combined cohort. Of those with detected significant COPD, 76% had no previous COPD diagnosis, 20% had eosinophil count 300/mm3, 15% were receiving inhaled corticosteroids and 65% had CAT >10.

Conclusions
Assessed by microspirometry in a large cohort of European patients, the prevalence of significant COPD in those hospitalised for acute MI with a significant smoking history was 18%. Symptom burden was high and treatment rates with ICS low. There were a large proportion of previously undiagnosed cases.

Measures for increased physical activity level and associations with health status and exacerbations in Chronic Obstructive Pulmonary Disease – a cohort study

Jenny Höglund[1], Gabriella Eliason[1], Maaike Giezeman[1], Mikael Hasselgren[1], Christer Jansson[2], Marta A Kisiel[2], Karin Lisspers[2], Scott Montgomery[1], Anna Nager[3], Hanna Sandelowsky[3], Björn Ställberg[1,2], Josefin Sundh[1]

[1] Örebro Universitet, [2] Uppsala Universitet, [3] Karolinska Institutet

Background

The importance of increasing the physical activity level in patients with Chronic Obstructive Pulmonary Disease (COPD) is highlighted in both national and international guidelines. In clinical practice different interventions are used to increase the physical activity level, but it is still unclear if this decreases the risk for symptoms and exacerbations. This cohort study aimed to analyze associations of physical activity level and measures to increase activity with exacerbations and COPD Assessement Test (CAT) score, in patients with COPD in mid-Sweden.

Method

Data from randomly selected patients with COPD in all stages were collected in 2014 within the PRAXIS-study, with follow-up in 2022. Data on self-reported patient characteristics, physical activity level, physiotherapist contact, CAT and exacerbations, were obtained from questionnaires. Information on spirometries and of advice on physical activity or referral to physiotherapist from asthma/COPD nurses were collected from medical records. Associations of self-reported physical activity level, established physiotherapist contact and measures from asthma/COPD nurses with CAT score and exacerbation status in 2022, were analysed using multivariable linear and, respectively, logistic regression. Adjustments were made for sex, age, body mass index (BMI), educational level, lung function, smoking status and baseline data of CAT score and exacerbations.

Results

Complete data were available in 535 patients: 56 % women, mean age 66.4 years, BMI 27. Established contact with physiotherapist in 2014 was independently associated with lower risk for having exacerbations in 2022 (OR [95%CI] 0.39 [0.17 to 0.89], p = 0.025).

Conclusion

Physiotherapist contact decreases the risk for future exacerbations, and should always be considered in patients with COPD.

The value of health status instruments (mMRC, CAT, and CCQ) in prediction of COPD exacerbations - the TIE cohort study

Andreas Palm[1], Kristina Bröms[2], Jens Ellingsen[1], Amir Farkhooy[1], Margareta Gonzalez-Lindh[2], Karin Lispers[3], Andrei Malinovschi[1], Björn Ställberg[3], Xingwu Zhou[3], Juan Wang[3], Marianne Högman[3], Maria Hårdstedt[4]

[1] Akademiska sjukhuset, [2] Centrum för forskning och utveckling, Gävle sjukhus, [3] Uppsala universitet, [4] Centrum för klinisk forskning, Falu lasarett

Background and aims: Identifying patients at risk for acute exacerbations of COPD (AECOPD) is crucial to improve care and outcomes. We aimed to evaluate the ability of three commonly used health status instruments to predict AECOPDs.

Methods: A prospective study including COPD patients in 2014–2016 - the Swedish Tools for Identifying Exacerbations in COPD (TIE) cohort study. AECOPDs were assessed from medical records one year before until three years after inclusion. Instruments evaluated were the modified Medical Research Council dyspnea scale (mMRC), the COPD Assessment Test (CAT) and the Clinical COPD Questionnaire (CCQ). Thresholds for prediction of AECOPDs were estimated using receiver operator characteristic curves. Unadjusted and adjusted Cox proportional hazards regressions assessed the predictive value of each instrument and combinations of instruments. Factors adjusted for: age, sex, BMI, current smoking status, FEV1 (% predicted) and AECOPD history the year before inclusion.

Results: In total, 572 patients (59% women, age 69±8 years, FEV1 57±18% of predicted) were included. Thresholds for predicting AECOPD during follow-up were estimated to ≥2 for mMRC, ≥13 for CAT, and ≥1.55 for CCQ. The adjusted HR (aHR) for prediction of AECOPD was for mMRC 1.6 (95% CI: 1.2–2.1), CAT 1.8 (1.4–2.3), and CCQ 1.6 (1.2–2.2). Compared to only one instrument above the threshold, aHR was 1.1 (0.7-1.7) and 1.4 (1.0-2.1) for two or three instruments above the threshold, respectively. A history of AECOPD had aHR of 2.7 (2.1–3.5), and each 10%-units decrease of FEV1 had aHR of 1.2 (1.1-1.3)).

Conclusion: mMRC, CAT, and CCQ independently predicted AECOPDs, and a combination of instruments tended to improve the accuracy of predictions. A history of exacerbations and impaired lung function were strong predictors of AECOPDs.