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CHRONIC OBSTRUCTIVE PULMONARY DISEASE:

Clinical phenotyping, mortality and causes of death

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Akademisk avhandling

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Abstract

Aim: To identify clinical relevant COPD phenotypes in a population-based study, using spirometry in combination with clinical characteristics and comorbidities, in relation to prognosis, assessed as mortality and also causes of death. **Methods:** A total of 993 individuals with airway obstruction ($FEV_1/VC < 0.70$) were identified after re-examinations of population-based cohorts in 2002-2004, together with age- and sex-matched non-obstructive referents. The cross-sectional data from 2002-2004 were used together with mortality data from the Swedish Tax Agency. Data on cause of death was collected from the Swedish National Board for Health and Welfare register, for all deaths until the 31st of December 2015. The following spirometric groups were used, in paper I: non-COPD ($FEV_1/VC \geq 0.70$); COPD (pre-bronchodilator (BD) $FEV_1/VC < 0.70$); in paper II, non-COPD as defined in paper I, obstructive divided into pre- not post-BD obstructive and post-BD obstructive (COPD); in paper III: Normal Lung Function (NLF, $FEV_1/VC \geq 0.7$ and $FVC \geq 80\%$ predicted), COPD (post-BD $FEV_1/VC < 0.70$) and COPD according to the Lower Limit of Normal criterion (LLN-COPD, post-BD FEV_1/VC below the lower fifth percentile derived from a reference population); in paper IV: NLF and COPD as defined in paper III, Restrictive Spirometric pattern (RSP, $FEV_1/VC \geq 0.70$ and $FVC < 80\%$ predicted). **Results:** Paper I: Productive cough was more common in COPD than non-COPD, and more common in men than in women. Productive cough increased the risk for exacerbations in COPD as well in non-COPD and was associated with worse survival in both groups. Men with COPD and productive cough had an increased risk for death by 63% when compared with non-COPD without productive cough, independent of the confounders, while among women, the 23% increased risk did not reach statistical significance. Paper II: Every fourth subject was misclassified as having COPD when the pre- BD spirometry was used. Subjects with pre- not post-BD obstruction reported 'any respiratory symptoms', asthma, exacerbations, and comorbidities similarly as those with COPD. Cumulative mortality among subjects with pre-not post-BD obstruction was lower than in COPD and but similar to non-obstructive. COPD, but not pre-not post-BD obstruction, was associated with an increased risk for death (HR;95%CI) when compared with non-obstructive, also in an adjusted model, 1.24;1.04-1.49, with a similar pattern among men and women (1.27;1.00-1.60 and 1.24;0.92-1.13). Paper III: Men with COPD had more cardiovascular disease (CVD) compared to women, while anxiety/depression (A/D) was more common among women. Still, CVD seemed to have a greater impact on death among women and A/D increased the risk of death in both sexes. CVD and A/D increased the risk for death among women, independently of confounders, while DM and A/D increased the risk among men. Applying the LLN criterion did not change the observed pattern. Paper IV: The most common cause of death in all groups was CVD, followed by cancer. COPD and RSP had a similar and higher mortality than NLF. RSP and COPD both had an increased risk for respiratory and CVD death compared to NLF, independent of confounders, however, non-significantly so for CVD in RSP. In all groups, the risk for deaths due to cancer was similar; although, lung cancer was more common in COPD compared to in NLF and RSP. **Conclusions:** Productive cough was common in COPD, and increased the risk for exacerbations in both sexes, in COPD as well as in non-COPD. The highest risk for exacerbations and death was found among subjects with both COPD and productive cough. Respiratory symptoms cannot distinguish COPD from pre- not post-BD obstruction. COPD but not pre- not post-BD obstruction had an increased the risk for death, when compared with non-obstructive, similarly among men and women. Even though CVD was more common among men, it had a greater impact on mortality among women, while A/D was more common among women, but had a similar impact on mortality in both sexes. RSP and COPD had a similar and worse survival compared with NLF. RSP and COPD had an increased risk for both CVD and respiratory death compared to NLF, while the risk for cancer- mortality was similar for all groups.

Keywords

Cardiovascular disease, causes of death, comorbidity, COPD, epidemiology, phenotype, mortality spirometry.

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