

Influence of *Pseudomonas aeruginosa* on the prognosis of Chronic Obstructive Pulmonary Disease (COPD)

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A retrospective cohort study of patients with COPD in the period between 2008-2018.

Background:

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world and represents an important public health challenge (1,2). The course of COPD is complicated by recurrent acute exacerbations (AECOPD), which impair health status, accelerate the decline of lung function and worsen the prognosis (3).

Pseudomonas aeruginosa (*P. aeruginosa*) is detected in the airways in up to 20% of the patients with acute exacerbation of COPD (5-11). The bacterium is more likely to be isolated from patients with more advanced disease and is associated with prolonged hospitalization, increased exacerbation rate and poor long-term prognosis compared to other microorganisms (12,13).

It is, however, difficult to draw definitive conclusions regarding the extent to which *P. aeruginosa* contributes to adverse clinical outcomes since severely reduced lung function is by itself a strong predictor of mortality in patients with COPD (14,15). Infection with *P. aeruginosa* might therefore be secondary to damaged lung tissue and decreased lung function, and thereby have no independent impact on the prognosis.

So far, no larger retrospective cohort study has been investigating the association between *P. aeruginosa* and prognosis in an unselected population of patients with COPD.

Aim of the study:

To investigate if *P. aeruginosa* is an independent predictor of disease progression, exacerbation and mortality in COPD in a nationwide and unselected database study.

Material and methods:

Retrospective cohort-study of patients enrolled in the Danish COPD database (Dansk Register for KOL; Dr-KOL) during January 2008 – January 2018.

Inclusion criteria:

- Verified COPD
- Age \geq 40 years

Exposure: Culture verified *P. aeruginosa* from lower respiratory tract specimens.

Data is collected from following databases:

Danish COPD database (Dr-KOL), Danish Microbiology Database (MiBa), The Danish National Health Data Authority (Sundhedsdatastyrelsen) and the Danish National Prescription Registry (Den Danske Receptdatabase).

Primary end-point:

- Time to exacerbation and/or death within 5 years from the *P. aeruginosa*-positive airway-culture.

Secondary main end-points:

- Frequency of exacerbation and/or death (all-cause) within 5 years.
- Frequency of hospital admission within 5 years.
- Frequency of hospital admission with non-invasive ventilation (NIV) or respiratory therapy during hospitalization within 5 years.
- Change in FEV1 (liter), CAT and BMI from baseline to 5 years.

Statistical analysis:

Cox proportional hazards regression will be used to analyse primary composite end-point in patients exposed to *P. aeruginosa*.

Funding and approval:

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Referencer:

1. Løkke et. al. Forekomst af kronisk obstruktiv lungesygdom i København: Resultater fra Østerbroundersøgelsen. Ugeskr Lager 2007;169(46):3956.
2. Jensen KB. Langt flere tilfælde af KOL end hidtil antaget. Ugeskr læger 2005; 167 (14): 1554.
3. Global Strategy for Diagnosis, Management, and Prevention of COPD: <http://www.goldcopd.org>.
4. Statens Institut for Folkesundhed (SIF). Folkesundhedsrapporten Danmark 2007: www.si-folkesundhed.dk.
5. Miravittles et al. Relationship between bacterial flora in sputum and functional impairment in patients with AECOPD. Chest 1999; 116:40-46
6. Alamoudi et al. Bacterial infection and risk factors in outpatients with AECOPD. Respirology 2007; 12:283-287
7. Ko et al. A 1-year prospective study of the infectious etiology in patients hospitalized with AECOPD. Chest 2007;131:44-52
8. Lin et al. Sputum bacteriology in hospitalized patients with AECOPD in Taiwan. Respirology 2007;12:81-87
9. Groenenwegen et al. Bacterial infections in patients requiring admission for AECOPD; a 1-year prospective study. Respiratory medicine 2003;97:770-777
10. Patel et al. Relationship between bacterial colonisation and the frequency, character and severity of COPD exacerbations. Thorax 2002;57:759-764
11. Renom et al. Prognosis of COPD patients requiring frequent hospitalization: role of airway infection. Respiratory medicine 2010;104:840-848
12. Garcia-Vidal et al. Pseudomonas aeruginosa in patients hospitalized for COPD exacerbation: a prospective study. European respiratory journal 2009;34:1072-1078
13. Almagro et al. Pseudomonas aeruginosa and mortality after hospital admission for COPD. Respiration 2012; 84:36-43
14. Murphy et al. Pseudomonas aeruginosa in COPD. Am J Respir Crit Care Med 2008;177:853-860
15. Rakhimova et al. Pseudomonas aeruginosa population biology in COPD. J of Infec Disease 2009;200:1928-35