LOW-DOSE CT SCREENING (LCS) FOR LUNG CANCER REDUCES 10-YEAR LUNG CANCER MORTALITY

The outcome of the Dutch-Belgian Nederlands-Leuven's Longkanker Screenings Onderzoek (NELSON) trial has been much anticipated. Powered to detect a mortality benefit of LCS in patients at high risk of lung cancer, De Koning et al (In Engl J Med 2020; 382:503) report the lung cancer mortality results after 10-year follow-up of participants enrolled to NELSON, a population-based, LCS randomised controlled trial. The primary analysis included 13,395 men, with a subgroup analysis in 2,594 women, aged 50–74 years who were current or former smokers. Patients were randomised 1:1 to receive four CT screening rounds (at baseline, 1, 3 and 5.5 years) or no screening. Data on lung cancer diagnosis and death were collected through National Registries. Lung cancer mortality was significantly lower in those who underwent CT screening compared with no screening, with benefits higher than previously demonstrated. In men, a 24% reduction in lung cancer mortality at 10 years was seen in the screened group compared with the control (rate ratio (RR) 0.76, 95% CI 0.61 to 0.94, p=0.01). The subgroup analysis in women suggests an even greater benefit of up to 33% (RR 0.67, 95% CI 0.38 to 1.14). The results support CT screening in high-risk groups; how policy-makers decide to take this forward awaits to be seen.

INHALED CORTICOSTEROID (ICS) USE DOES NOT DECREASE THE INCIDENCE OF LUNG CANCER IN COPD

Observational data have suggested a possible beneficial impact of ICS on the incidence of lung cancer, however, the reported results have been inconsistent. Suissa and colleagues (Eur Respir J 2020; DOI: 10.1183/13993003.01720-2019) report results from a well-designed observational cohort study assessing the association between ICS use and lung cancer incidence. Using health databases from Quebec, 63,726 patients with COPD aged ≥50 years who were new users of long-acting bronchodilators (long-acting muscarinic antagonists (LAMAs) or long acting β₂-agonists (LABAs) without ICS) between the years 2000 and 2014 were identified. Subjects were excluded if they had a prescription for ICS in the year prior to cohort entry. Subjects were followed until the end of the study (mean follow-up time 4.7 years) for a first diagnosis of lung cancer and data collected on ICS use in the follow-up period. A time-dependent Cox regression model was used to estimate the HR of lung cancer associated with ICS exposure. The authors demonstrate that ICS use in patients with COPD is not associated with a reduction in lung cancer incidence (HR 1.01, 95% CI 0.94 to 1.08). Additionally, while duration of use had no effect, higher doses were associated with a higher incidence of lung cancer (HR 1.36, 95% CI 1.03 to 1.81). Previous studies may have been confounded by inclusion of patients with asthma and time-related biases. The authors conclude that the need for any future placebo-based randomised trial must be carefully considered in light of their study findings.

COPD COMORBIDITIES IMPACT ON SURVIVAL

Mortality in COPD is partly attributed to comorbidities. Whether pharmacological treatment has a role in impacting mortality in COPD is unclear. Ellingsen and colleagues (Int J Chron Obstruct Pulmon Dis 2020;15:235) report results from a retrospective, observational, population-based study of patients with COPD in Sweden. All-cause mortality was analysed in a cohort of 17,745 patients with physician-diagnosed COPD between 1999 and 2009 identified through primary care centres. Using National Registries, data were collected on socioeconomic factors, exacerbations, comorbidities and medications. A total of 8,776 subjects (32.5%) died during the observation period. Comorbidities were associated with increased mortality in patients with COPD, including heart failure (HR 1.88, 95% CI 1.74 to 2.04), stroke (HR 1.52, 95% CI 1.40 to 1.64) and myocardial infarction (HR 1.40, 95% CI 1.24 to 1.58). Interestingly, the use of a LAMA was associated with increased mortality (HR 1.33, 95% CI 1.14 to 1.55), while ICS therapy was associated with an improved prognosis (HR 0.79, 95% CI 0.66 to 0.94). However, data on COPD phenotype or lung function impairment were not available and so may confound the results. In an era of increasingly specialised medical practice, the data remind the clinician that a holistic approach to management of patients with COPD may reap benefits.

IS THERE A ROLE FOR BENRALIZUMAB IN COPD?

While indicated for add-on maintenance treatment of severe eosinophilic asthma, benralizumab did not significantly reduce exacerbations in patients with COPD compared with placebo in the phase 3, industry-funded, GALATHEA and TERRANOVA trials. Criner et al (Lancet Respir Med 2020;8:158) set out to identify clinical characteristics of participating patients who may benefit from benralizumab. The analysis had been a priori stipulated in the trial protocols. Pooled and individual results from the GALATHEA and TERRANOVA trials of 3,910 patients aged 40–85 years with moderate to very severe airflow limitation, elevated blood eosinophils and two or more exacerbations or one or more severe exacerbation in the past year despite dual or triple inhaled therapy were analysed. Patients received benralizumab (30 mg or 100 mg subcutaneously every 8 weeks; first three doses every 4 weeks) or placebo. Patients with baseline blood eosinophils of ≥220 cells/μL, with three or more exacerbations in the previous year and receiving triple therapy were demonstrated to have a decreased frequency of exacerbations with benralizumab 100 mg versus placebo (RR 0.70, 95% CI 0.56 to 0.88). The lower 30 mg dose did not confer any benefit in the same group compared with placebo (RR 0.99, 95% CI 0.79 to 1.23). As may be expected, the more frequent exacerbators had worse lung function and quality of life and had the diagnosis of COPD for longer than those with less frequent exacerbations. The authors identify a subgroup of patients with COPD who may benefit from the addition of antieosinophil therapy. These findings require prospective evaluation in the clinical trial setting.

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