Pulmonary Arterial Enlargement and Acute Exacerbations of COPD


Background. Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with accelerated loss of lung function and death. Identification of patients at risk for these events, particularly those requiring hospitalisation, is of major importance. Severe pulmonary hypertension is an important complication of advanced COPD and predicts acute exacerbations, though pulmonary vascular abnormalities also occur early in the course of the disease. We hypothesized that a computed tomographic (CT) metric of pulmonary vascular disease (pulmonary artery enlargement, as determined by a ratio of the diameter of the pulmonary artery to the diameter of the aorta [PA:A ratio] of >1) would be associated with severe COPD exacerbations.

Methods. We conducted a multicenter, observational trial that enrolled current and former smokers with COPD. We determined the association between a PA:A ratio of more than 1 and a history at enrollment of severe exacerbations requiring hospitalisation and then examined the usefulness of the ratio as a predictor of these events in a longitudinal follow-up of this cohort, as well as in an external validation cohort. We used logistic-regression and zero-inflated negative binomial regression analyses and adjusted for known risk factors for exacerbation.

Results. Multivariate logistic-regression analysis showed a significant association between a PA:A ratio of more than 1 and a history of severe exacerbations at the time of enrollment in the trial (odds ratio, 4.78; 95% confidence interval [CI], 3.43 to 6.65; P<0.001). A PA:A ratio of more than 1 was also independently associated with an increased risk of future severe exacerbations in both the trial cohort (odds ratio, 3.44; 95% CI, 2.78 to 4.25; P<0.001) and the external validation cohort (odds ratio, 2.80; 95% CI, 2.11 to 3.71; P<0.001). In both cohorts, among all the variables analyzed, a PA:A ratio of more than 1 had the strongest association with severe exacerbations.

Conclusion. Pulmonary artery enlargement (a PA:A ratio of >1), as detected by CT, was associated with severe exacerbations of COPD. (Funded by the National Heart, Lung, and Blood Institute; ClinicalTrials.gov numbers, NCT00608764 and NCT00292552.)

Effect of Inhaled Glucocorticoids in Childhood on Adult Height

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Background. The use of inhaled glucocorticoids for persistent asthma causes a temporary reduction in growth velocity in prepubertal children. The resulting decrease in attained height 1 to 4 years after the initiation of inhaled glucocorticoids is thought not to decrease attained adult height.

Methods. We measured adult height in 943 of 1041 participants (90.6%) in the Childhood Asthma Management Program; adult height was determined at a mean (±SD) age of 24.9±2.7 years. Starting at the age of 5 to 13 years, the participants had been randomly assigned to receive 400 μg of budesonide, 16 mg of nedocromil, or placebo daily for 4 to 6 years. We calculated differences in adult height for each active treatment group, as compared with placebo, using multiple linear regression with adjustment for demographic characteristics, asthma features, and height at trial entry.

Results. Mean adult height was 1.2 cm lower (95% confidence interval [CI], –1.9 to –0.5) in the...
budesonide group than in the placebo group (P=0.001) and was 0.2 cm lower (95% CI, –0.9 to 0.5) in the nedocromil group than in the placebo group (P=0.61). A larger daily dose of inhaled glucocorticoid in the first 2 years was associated with a lower adult height (–0.1 cm for each microgram per kilogram of body weight) (P=0.007). The reduction in adult height in the budesonide group as compared with the placebo group was similar to that seen after 2 years of treatment (–1.3 cm; 95% CI, –1.7 to –0.9). During the first 2 years, decreased growth velocity in the budesonide group occurred primarily in prepubertal participants.

Conclusions. The initial decrease in attained height associated with the use of inhaled glucocorticoids in prepubertal children persisted as a reduction in adult height, although the decrease was not progressive or cumulative. (Funded by the National Heart, Lung, and Blood Institute and the National Center for Research Resources; CAMP ClinicalTrials.gov number, NCT00000575.)

A Randomized Study of How Physicians Interpret Research Funding Disclosures

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Background. The effects of clinical-trial funding on the interpretation of trial results are poorly understood. We examined how such support affects physicians’ reactions to trials with a high, medium, or low level of methodologic rigor.

Methods. We presented 503 board-certified internists with abstracts that we designed describing clinical trials of three hypothetical drugs. The trials had high, medium, or low methodologic rigor, and each report included one of three support disclosures: funding from a pharmaceutical company, NIH funding, or none. For both factors studied (rigor and funding), one of the three possible variations was randomly selected for inclusion in the abstracts. Follow-up questions assessed the physicians’ impressions of the trials’ rigor, their confidence in the results, and their willingness to prescribe the drugs.

Results. The 269 respondents (53.5% response rate) perceived the level of study rigor accurately. Physicians reported that they would be less willing to prescribe drugs tested in low-rigor trials than those tested in medium-rigor trials (odds ratio, 0.64; 95% CI, 0.46 to 0.89; P=0.008) and would be more willing to prescribe drugs tested in high-rigor trials than those tested in medium-rigor trials (odds ratio, 3.07; 95% CI, 2.18 to 4.32; P<0.001). Disclosure of industry funding, as compared with no disclosure of funding, led physicians to downgrade the rigor of a trial (odds ratio, 0.63; 95% CI, 0.46 to 0.87; P=0.006), their confidence in the results (odds ratio, 0.71; 95% CI, 0.51 to 0.98; P=0.04), and their willingness to prescribe the hypothetical drugs (odds ratio, 0.68; 95% CI, 0.49 to 0.94; P=0.02). Physicians were half as willing to prescribe drugs studied in industry-funded trials as they were to prescribe drugs studied in NIH-funded trials (odds ratio, 0.52; 95% CI, 0.37 to 0.71; P<0.001). These effects were consistent across all levels of methodologic rigor.

Conclusions. Physicians discriminate among trials of varying degrees of rigor, but industry sponsorship negatively influences their perception of methodologic quality and reduces their willingness to believe and act on trial findings, independently of the trial’s quality. These effects may influence the translation of clinical research into practice.

Patients' Expectations About Effects of Chemotherapy for Advanced Cancer

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Background. Chemotherapy for metastatic lung or colorectal cancer can prolong life by weeks or months and may provide palliation, but it is not curative.

Methods. We studied 1193 patients participating in the Cancer Care Outcomes Research and Surveillance (CanCORS) study (a national, prospective,
observational cohort study) who were alive 4 months after diagnosis and received chemotherapy for newly diagnosed metastatic (stage IV) lung or colorectal cancer. We sought to characterize the prevalence of the expectation that chemotherapy might be curative and to identify the clinical, sociodemographic, and health-system factors associated with this expectation. Data were obtained from a patient survey by professional interviewers in addition to a comprehensive review of medical records.

**Results.** Overall, 69% of patients with lung cancer and 81% of those with colorectal cancer did not report understanding that chemotherapy was not at all likely to cure their cancer. In multivariable logistic regression, the risk of reporting inaccurate beliefs about chemotherapy was higher among patients with colorectal cancer, as compared with those with lung cancer (odds ratio, 1.75; 95% confidence interval [CI], 1.29 to 2.37); among nonwhite and Hispanic patients, as compared with non-Hispanic white patients (odds ratio for Hispanic patients, 2.82; 95% CI, 1.51 to 5.27; odds ratio for black patients, 2.93; 95% CI, 1.80 to 4.78); and among patients who rated their communication with their physician very favorably, as compared with less favorably (odds ratio for highest third vs. lowest third, 1.90; 95% CI, 1.33 to 2.72). Educational level, functional status, and the patient’s role in decision making were not associated with such inaccurate beliefs about chemotherapy.

**Conclusions.** Many patients receiving chemotherapy for incurable cancers may not understand that chemotherapy is unlikely to be curative, which could compromise their ability to make informed treatment decisions that are consonant with their preferences. Physicians may be able to improve patients’ understanding, but this may come at the cost of patients’ satisfaction with them. (Funded by the National Cancer Institute and others.)