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Abstracts' Service

Antibiotic Therapy and Treatment Failure in Patients Hospitalized for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Context. Guidelines recommend antibiotic therapy for acute exacerbations of chronic obstructive pulmonary disease (COPD), but the evidence is based on small, heterogeneous trials, few of which include hospitalized patients.

Objective. To compare the outcomes of patients treated with antibiotics in the first 2 hospital days with those treated later or not at all.

Design, Setting, and Patients. Retrospective cohort of patients aged 40 years or older who were hospitalized from January 1, 2006, through December 31, 2007, for acute exacerbations of COPD at 413 acute care facilities throughout the United States.

Main Outcome Measures. A composite measure of treatment failure, defined as the initiation of mechanical ventilation after the second hospital day, inpatient mortality, or readmission for acute exacerbations of COPD within 30 days of discharge; length of stay and hospital costs.

Result. Of 84 621 patients, 79% received at least 2 consecutive days of antibiotic treatment. Treated patients were less likely than nontreated patients to receive mechanical ventilation after the second hospital day (1.07%; 95% confidence interval [CI], 1.06%-1.08% vs 1.80%; 95% CI, 1.78%-1.82%), had lower rates of inpatient mortality (1.04%; 95% CI, 1.03%-1.05% vs 1.59%; 95% CI, 1.57%-1.61%), and had lower rates of readmission for acute exacerbations of COPD (7.91%; 95% CI, 7.89%-7.94% vs 8.79%; 95% CI, 8.74%-8.83%). Patients treated with antibiotic agents had a higher rate of readmissions for *Clostridium difficile* (0.19%; 95% CI, 0.187%-0.193%) than those who were not treated (0.09%; 95% CI, 0.086%-0.094%). After multivariable adjustment, including the propensity for antibiotic treatment, the risk of treatment failure was lower in antibiotic-treated patients (odds ratio, 0.87; 95% CI, 0.82-0.92). A grouped treatment approach and hierarchical modeling to account for potential confounding of hospital effects yielded similar results. Analysis stratified by risk of treatment failure found similar magnitudes of benefit across all subgroups.

Conclusion. Early antibiotic administration was associated with improved outcomes among patients hospitalized for acute exacerbations of COPD regardless of the risk of treatment failure.

Reporting and Interpretation of Randomized Controlled Trials with Statistically Nonsignificant Results for Primary Outcomes

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Context. Previous studies indicate that the interpretation of trial results can be distorted by authors of published reports.

Objective. To identify the nature and frequency of distorted presentation or "spin" (ie, specific reporting strategies, whatever their motive, to highlight that the experimental treatment is beneficial, despite a statistically nonsignificant difference for the primary outcome, or to distract the reader from statistically nonsignificant results) in published reports of randomized controlled trials (RCTs) with statistically nonsignificant results for primary outcomes.

Data Sources. March 2007 search of MEDLINE via PubMed using the Cochrane Highly Sensitive Search Strategy to identify reports of RCTs published in December 2006.

Study Selection. Articles were included if they were parallel-group RCTs with a clearly identified primary outcome showing statistically nonsignificant results (ie, $p \geq .05$).

Data Extraction. Two readers appraised each selected article using a pretested, standardized data abstraction form developed in a pilot test.

Results. From the 616 published reports of RCTs

examined, 72 were eligible and appraised. The title was reported with spin in 13 articles (18.0%; 95% confidence interval [CI], 10.0%-28.9%). Spin was identified in the Results and Conclusions sections of the abstracts of 27 (37.5%; 95% CI, 26.4%-49.7%) and 42 (58.3%; 95% CI, 46.1%-69.8%) reports, respectively, with the conclusions of 17 (23.6%; 95% CI, 14.4%-35.1%) focusing only on treatment effectiveness. Spin was identified in the main-text Results, Discussion, and Conclusions sections of 21 (29.2%; 95% CI, 19.0%-41.1%), 31 (43.1%; 95% CI, 31.4%-55.3%), and 36 (50.0%; 95% CI, 38.0%-62.0%) reports, respectively. More than 40% of the reports had spin in at least 2 of these sections in the main text.

Conclusion. In this representative sample of RCTs published in 2006 with statistically nonsignificant primary outcomes, the reporting and interpretation of findings was frequently inconsistent with the results.

Association of Corticosteroid Dose and Route of Administration with Risk of Treatment Failure in Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Context. Systemic corticosteroids are beneficial for patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease (COPD); however, their optimal dose and route of administration are uncertain.

Objective. To compare the outcomes of patients treated with low doses of steroids administered orally to those treated with higher doses administered intravenously.

Design, Setting and Patients. A pharmaco-epidemiological cohort study conducted at 414 US hospitals involving patients admitted with acute exacerbation of COPD in 2006 and 2007 to a non-intensive care setting and who received systemic corticosteroids during the first 2 hospital days.

Main Outcome Measures. A composite measure of treatment failure, defined as the initiation of mechanical ventilation after the second hospital day, inpatient mortality, or readmission for acute exacerbation of COPD within 30 days of discharge. Length of stay and hospital costs.

Results. Of 79 985 patients, 73 765 (92%) were initially treated with intravenous steroids, whereas 6220 (8%) received oral treatment. We found that 1.4% (95% confidence interval [CI], 1.3%-1.5%) of the intravenously and 1.0% (95% CI, 0.7%-1.2%) of the orally treated patients died during hospitalization, whereas 10.9% (95% CI, 10.7%-11.1%) of the intravenously and 10.3% (95% CI, 9.5%-11.0%) of the orally treated patients experienced the composite outcome. After multivariable adjustment, including the propensity for oral treatment, the risk of treatment failure among patients treated orally was not worse than for those treated intravenously (odds ratio [OR], 0.93; 95% CI, 0.84-1.02). In a propensity-matched analysis, the risk of treatment failure was significantly lower among orally treated patients (OR, 0.84; 95% CI, 0.75-0.95), as was length of stay and cost. Using an adaptation of the instrumental variable approach, increased rate of treatment with oral steroids was not associated with a change in the risk of treatment failure (OR for each 10% increase in hospital use of oral steroids, 1.00; 95% CI, 0.97-1.03). A total of 1356 (22%) patients initially treated with oral steroids were switched to intravenous therapy later in the hospitalization.

Conclusion. Among patients hospitalized for acute exacerbation of COPD low-dose steroids administered orally are not associated with worse outcomes than high-dose intravenous therapy.

Association Between Respiratory Tract Methicillin-Resistant *Staphylococcus aureus* and Survival in Cystic Fibrosis

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Context. The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in the respiratory tract of individuals with cystic fibrosis (CF) has increased dramatically; however, its impact on outcomes in CF is

unclear. Because the time between infection with bacteria in CF and death can be decades, observational studies with long periods of follow-up are well suited to address the current gap in knowledge.

Objective. To determine whether isolation of MRSA from the respiratory tract of CF patients is associated with worse survival compared with patients who never have a culture positive for MRSA.

Design, Setting and Participants. Cohort study of 19 833 CF patients aged 6 to 45 years seen at centers accredited by the Cystic Fibrosis Foundation in the United States. Patients entered between January 1996 and December 2006 and were followed up through December 2008. Cox regression models with time-varying covariates were used to compare survival between CF patients with and without respiratory tract MRSA.

Main Outcome Measure. Time from age at entry until age at death from any cause.

Results. In 137 819 patient-years of observation (median, 7.3 years/patient), 2537 CF patients died and 5759 patients had MRSA detected. The mortality rate was 18.3 deaths (95% confidence interval [CI], 17.5-19.1) per 1000 patient-years in patients without MRSA and 27.7 deaths (95% CI, 25.3-30.4) per 1000 patient-years in those with MRSA. Among those with MRSA, the attributable risk percentage of death associated with MRSA was 34.0% (95% CI, 26.7-40.4%). The unadjusted hazard ratio associated with MRSA was 1.47 (95% CI, 1.32-1.62). After adjustment for time-varying covariates associated with severity of illness, MRSA remained associated with a higher risk of death (1.27; 95% CI, 1.11-1.45).

Conclusion. Detection of MRSA in the respiratory tract of CF patients was associated with worse survival.

Endobronchial Ultrasound Increases the Diagnostic Yields of Polymerase Chain Reaction and Smear for Pulmonary Tuberculosis

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Objectives. Our objective was to determine the contribution of endobronchial ultrasound in the diagnostic yields of acid-fact bacillus smear, nucleic acid amplification tests, and culture in bronchoalveolar lavage fluid for pulmonary tuberculosis.

Methods. During a 1-year interval, 99 patients who had initial sputum-negative acid-fast bacillus smears or no sputum but were later proven to have a positive culture for *Mycobacterium tuberculosis* in their sputum or bronchoalveolar lavage fluid were retrospectively studied. Among them, 56 patients underwent bronchoscopy with endobronchial ultrasound (EBUS group) and 43 patients received conventional bronchoscopy for bronchoalveolar lavage (non-EBUS group).

Results. The diagnostic yields of the nucleic acid amplification tests (89.3%, 50/56; $P = .006$), acid-fast bacillus smear (30.4%, 17/56; $P = .013$), *M tuberculosis* culture in bronchoalveolar lavage fluid (67.9%, 38/56; $P = .041$) were significantly higher in the EBUS group of patients. The results of those who underwent conventional bronchoscopy were 65.1% (28/43), 9.3% (4/43), and 46.5% (20/43), respectively. Combining bronchoalveolar lavage fluid smear and nucleic acid amplification tests, we made a rapid diagnosis of pulmonary tuberculosis in 51 (91.1%) of the 56 EBUS patients and 29 (67.4%; $P = .004$) of the 43 non-EBUS patients.

Conclusions. The introduction of endobronchial ultrasound increases the diagnostic yield of the nucleic acid amplification tests, acid-fast bacillus smear, and *M. tuberculosis* culture from bronchoalveolar lavage fluid in patients with pulmonary tuberculosis who have negative sputum smear or no sputum production.

Pneumonectomy is a Valuable Treatment Option after Neoadjuvant Therapy for Stage III Non-Small-Cell Lung Cancer

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Objective. The mortality of pneumonectomy after chemotherapy or chemoradiotherapy for locally advanced non-small-cell lung cancer is reported to be as high as 26%. We retrospectively reviewed the

medical records of patients undergoing these procedures in 2 specialized thoracic centers to determine the outcome.

Methods. Retrospective analyses were performed of all patients who underwent pneumonectomy after neoadjuvant chemotherapy or chemoradiotherapy for locally advanced non-small-cell lung cancer from 1998 to 2007. Presurgical treatment consisted of 3-4 platin-based doublets alone in 20% of patients or combined with radiotherapy (45Gy) to the tumor and mediastinum in 80% of patients.

Results. Of 827 patients who underwent neoadjuvant therapy, 176 pneumonectomies were performed, including 138 (78%) extended resections. Post-induction pathologic stages were 0 in 36 patients (21%), I in 33 patients (19%), II in 38 patients (21%), III in 57 patients (32%), and IV in 12 patients (7%). Three patients died of pulmonary embolism, 2 patients of respiratory failure, and 1 patient of cardiac failure, resulting in a 90 postoperative day mortality rate of 3%; 23 major complications occurred in 22 patients (13%). For the overall population, 3-year survival was 43% and 5-year survival was 38%.

Conclusions. Pneumonectomy after neoadjuvant therapy for non-small-cell lung cancer can be performed with a perioperative mortality rate of 3%. Thus, the need of a pneumonectomy for complete resection alone should not be a reason to exclude patients from a potentially curative procedure if done in an experienced center. The 5-year survival of 38%, which can be achieved, justifies extended surgery within a multimodality concept for selected patients with locally advanced non-small-cell lung cancer.