Saudi COPD Group Newsletter

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VISION:

Prevention, earlier detection and providing the best medical care for patients with COPD will result in improved outcomes, quality of life and consequently a lower burden on the patients, their families, the healthcare system and the community.

MISSION:

To serve as a recognized group of excellence for a comprehensive, state of the art, evidence-based approach through providing scientific educational activities and research initiatives to healthcare professionals, patients with COPD and the general public.

BACKGROUND AND OBJECTIVES:

The Saudi COPD group is a scientific and educational group, working under the umbrella of the Saudi Thoracic Society (STS). The aim is to enhance awareness of COPD in healthcare professionals and increasing public health education regarding COPD for the patients and their families and in the community.

The objectives of the group will be achieved by organizing scientific educational activities, including conferences, seminars, courses and workshops for healthcare professionals and conducting public educational activities for the patients diagnosed with COPD in healthcare facilities or via social networks.

The group's members are physicians and others healthcare professionals with a deep interest and extensive experience in COPD diagnosis and management. They have a strong and continuous commitment to achieve the objectives of the group and improve the awareness of the disease and the quality of life of the patients with COPD.

The panel members of Saudi COPD group had selected the following recent papers from various journals related to all aspects of COPD hoping will be useful and helpful in your practice and patient care.

C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations:

SAUDI COPD GROUP

Background: Point-of-care testing of C-reactive protein (CRP) may be a way to reduce unnecessary use of antibiotics without harming patients who have acute exacerbations of chronic obstructive pulmonary disease (COPD).

Methods: We performed a multicenter, open-label, randomized, controlled trial involving patients with a diagnosis of COPD in their primary care clinical record who consulted a clinician at 1 of 86 general medical practices in England and Wales for an acute exacerbation of COPD. The patients were assigned to receive usual care guided by CRP point-of-care testing (CRP-guided group) or usual care alone (usual-care group). The primary outcomes were patient-reported use of antibiotics for acute exacerbations of COPD within 4 weeks after randomization (to show superiority) and COPD-related health status at 2 weeks after randomization, as measured by the Clinical COPD Questionnaire, a 10-item scale with scores ranging from 0 (very good COPD health status) to 6 (extremely poor COPD health status) (to show noninferiority).

Results: A total of 653 patients underwent randomization. Fewer patients in the CRP-guided group reported antibiotic use than in the usual-care group (57.0% vs. 77.4%; adjusted odds ratio, 0.31; 95% confidence interval [CI], 0.20 to 0.47). The adjusted mean difference in the total score on the Clinical COPD Questionnaire at 2 weeks was −0.19 points (two-sided 90% CI, −0.33 to −0.05) in favor of the CRP-guided group. The antibiotic prescribing decisions made by clinicians at the initial consultation were ascertained for all but 1 patient, and antibiotic prescriptions issued over the first 4 weeks of follow-up were ascertained for 96.9% of the patients. A lower percentage of patients in the CRP-guided group than in the usual-care group received an antibiotic prescription at the initial consultation (47.7% vs. 69.7%, for a difference of 22.0 percentage points; adjusted odds ratio, 0.31; 95% CI, 0.21 to 0.45) and during the first 4 weeks of follow-up (59.1% vs. 79.7%, for a difference of 20.6 percentage points; adjusted odds ratio, 0.30; 95% CI, 0.20 to 0.46). Two patients in the usual-care group died within 4 weeks after randomization from causes considered by the investigators to be unrelated to trial participation.

Conclusion: CRP-guided prescribing of antibiotics for exacerbations of COPD in primary care clinics resulted in a lower percentage of patients who reported antibiotic use and who received antibiotic prescriptions from clinicians, with no evidence of harm.

https://www.nejm.org/doi/full/10.1056/NEJMoa1803185

Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD

Background: Triple fixed-dose regimens of an inhaled glucocorticoid, a long-acting muscarinic antagonist (LAMA), and a long-acting β2-agonist (LABA) for chronic obstructive pulmonary disease (COPD) have been studied at single dose levels of inhaled glucocorticoid, but studies at two dose levels are lacking.

Methods: In a 52-week, phase 3, randomized trial to evaluate the efficacy and safety of triple therapy at two dose levels of inhaled glucocorticoid in patients with moderate-to-very-severe COPD and at least one exacerbation in the past year, we assigned patients in a 1:1:1:1 ratio to receive twice-daily inhaled doses of triple therapy (inhaled glucocorticoid [320 μg or 160 μg of budesonide], a LAMA [18 μg of glycopyrrolate], and a LABA [9.6 μg of formoterol]) or one of two dual therapies (18 μg of glycopyrrolate plus 9.6 μg of formoterol or 320 μg of budesonide plus 9.6 μg of formoterol). The primary end point was the annual rate (the estimated mean number per patient per year) of moderate or severe COPD exacerbations, as analyzed in the modified intention-to-treat population with the use of on-treatment data only.

Results: The modified intention-to-treat population comprised 8509 patients. The annual rates of moderate or severe exacerbations were 1.08 in the 320-μg–budesonide triple-therapy group (2137 patients), 1.07 in the 160-μg–budesonide triple-therapy group (2121 patients), 1.42 in the glycopyrrolate–formoterol group (2120 patients), and 1.24 in the budesonide–formoterol group (2131 patients). The rate was significantly lower with 320-μg–budesonide triple therapy than with glycopyrrolate–formoterol (24% lower: rate ratio, 0.76; 95% confidence interval [CI], 0.69 to 0.83; P<0.001) or budesonide–formoterol (13% lower: rate ratio, 0.87; 95% CI, 0.79 to 0.95; P=0.003). Similarly, the rate was significantly lower with 160-μg–budesonide triple therapy than with glycopyrrolate–formoterol (25% lower: rate ratio, 0.75; 95% CI, 0.69 to 0.83; P<0.001) or budesonide–formoterol (14% lower: rate ratio, 0.86; 95% CI, 0.79 to 0.95; P=0.002). The incidence of any adverse event was similar across the treatment groups (range, 61.7 to 64.5%); the incidence of confirmed pneumonia ranged from 3.5 to 4.5% in the groups that included inhaled glucocorticoid use and was 2.3% in the glycopyrrolate–formoterol group.

Conclusion: Triple therapy with twice-daily budesonide (at either the 160-μg or 320-μg dose), glycopyrrolate, and formoterol resulted in a lower rate of moderate or severe COPD exacerbations than glycopyrrolate–formoterol or budesonide–formoterol.

https://www.nejm.org/doi/full/10.1056/NEJMoa1916046

Importance: The prevalence of pulmonary embolism in patients with chronic obstructive pulmonary disease (COPD) and acutely worsening respiratory symptoms remains uncertain.

Objective: To determine the prevalence of pulmonary embolism in patients with COPD admitted to the hospital for acutely worsening respiratory symptoms.

Design, Setting, and Participants: Multicenter cross-sectional study with prospective follow-up conducted in 7 French hospitals. A predefined pulmonary embolism diagnostic algorithm based on Geneva score, D-dimer levels, and spiral computed tomographic pulmonary angiography plus leg compression ultrasound was applied within 48 hours of admission; all patients had 3-month follow-up. Patients were recruited from January 2014 to May 2017 and the final date of follow-up was August 22, 2017.

Exposures: Acutely worsening respiratory symptoms in patients with COPD.

Main Outcomes and Measures: The primary outcome was pulmonary embolism diagnosed within 48 hours of admission. Key secondary outcome was pulmonary embolism during a 3-month follow-up among patients deemed not to have venous thromboembolism at admission and who did not receive anticoagulant treatment. Other outcomes were venous thromboembolism (pulmonary embolism and/or deep vein thrombosis) at admission and during follow-up, and 3-month mortality, whether venous thromboembolism was clinically suspected or not.

Results: Among 740 included patients (mean age, 68.2 years [SD, 10.9 years]; 274 women [37.0%]), pulmonary embolism was confirmed within 48 hours of admission in 44 patients (5.9%; 95% CI, 4.5%-7.9%). Among the 670 patients deemed not to have venous thromboembolism at admission and who did not receive anticoagulation, pulmonary embolism occurred in 5 patients (0.7%; 95% CI, 0.3%-1.7%) during follow-up, including 3 deaths related to pulmonary embolism. The overall 3-month mortality rate was 6.8% (50 of 740; 95% CI, 5.2%-8.8%). The proportion of patients who died during follow-up was higher among those with venous thromboembolism at admission than the proportion of those without it at admission (14 [25.9%] of 54 patients vs 36 [5.2%] of 686; risk difference, 20.7%, 95% CI, 10.7%-33.8%; P < .001). The prevalence of venous thromboembolism was 11.7% (95% CI, 8.6%-15.9%) among patients in whom pulmonary embolism was suspected (n = 299) and was 4.3% (95% CI, 2.8%-6.6%) among those in whom pulmonary embolism was not suspected (n = 441).

Conclusions and Relevance: Among patients with chronic obstructive pulmonary disease admitted to the hospital with an acute worsening of respiratory symptoms, pulmonary embolism was detected in 5.9% of patients using a predefined diagnostic algorithm. Further research is needed to understand the possible role of systematic screening for pulmonary embolism in this patient population.

Importance: Morphine is used as palliative treatment of chronic breathlessness in patients with advanced chronic obstructive pulmonary disease (COPD). Evidence on respiratory adverse effects and health status is scarce and conflicting.

Objective: To assess the effects of regular, low-dose, oral sustained-release morphine on disease-specific health status (COPD Assessment Test; CAT), respiratory outcomes, and breathlessness in patients with COPD.

Interventions: Participants were randomly assigned to 10 mg of regular, oral sustained-release morphine or placebo twice daily for 4 weeks, with the possibility to increase to 3 times daily after 1 or 2 weeks.

Design, Setting, and Participants: the Morphine for Treatment of Dyspnea in Patients with COPD (MORDYC) study was a randomized, double-blind, and placebo-controlled study of a 4-week intervention. Patients were enrolled between November 1, 2016, and January 24, 2019. Participants were recruited in a pulmonary rehabilitation center and 2 general hospitals after completion of a pulmonary rehabilitation program. Outpatients with COPD and moderate to very severe chronic breathlessness (modified Medical Research Council [mMRC] breathlessness grades 2-4) despite optimal pharmacological and nonpharmacological treatment were included. A total of 1380 patients were screened, 916 were ineligible, and 340 declined to participate.

Main Outcomes and Measures: Primary outcomes were CAT score (higher scores represent worse health status) and arterial partial pressure of carbon dioxide (PaCO2). Secondary outcome was breathlessness in the previous 24 hours (numeric rating scale). Data were analyzed by intention to treat. Subgroup analyses in participants with mMRC grades 3 to 4 were performed.

Results: A total of 111 of 124 included participants were analyzed (mean [SD] age, 65.4 [8.0] years; 60 men [54%]). Difference in CAT score was 2.18 points lower in the morphine group (95% CI, −4.14 to −0.22 points; P = .03). Difference in PaCO2 was 1.19 mm Hg higher in the morphine group (95% CI, −2.70 to 5.07 mm Hg; P = .55). Breathlessness remained unchanged. Worst breathlessness improved in participants with mMRC grades 3 to 4 (1.33 points lower in the morphine group; 95% CI, −2.50 to −0.16 points; P = .03). Five participants of 54 in the morphine group (9%) and 1 participant of 57 in the placebo group (2%) withdrew because of adverse effects. No morphine-related hospital admissions or deaths occurred.

Conclusions and Relevance: In this randomized clinical trial, regular, low-dose, oral sustained-release morphine for 4 weeks improved disease-specific health status in patients with COPD without affecting PaCO2 or causing serious adverse effects. The worst breathlessness improved in participants with mMRC grades 3 to 4. A larger randomized clinical trial with longer follow-up in patients with mMRC grades 3 to 4 is warranted.

Prevalence, Pattern, Risks Factors and Consequences of Antibiotic Resistance in COPD: A Systematic Review

A concern of antibiotic use in chronic obstructive pulmonary disease (COPD) is the emergence and propagation of antimicrobial resistance (AMR). A systematic review was conducted to determine prevalence, pattern, risk factors and consequences of AMR in COPD. Bibliographic databases were searched from inception to November 2020, with no language restrictions, including studies of any design that included patients with COPD and reported prevalence and pattern of AMR. 2748 unique titles and abstracts were identified, of which 63 articles, comprising 26,387 patients, met inclusion criteria. Forty-four (69.8%) studies were performed during acute exacerbation. The median prevalence of AMR ranged from 0–100% for Pseudomonas aeruginosa, *Moraxella catarrhalis, Klebsiella pneumoniae and Acinetobacter baumannii*. Median resistance rates of *H influenzae and S pneumoniae* were lower by comparison, with maximum rates ≤40% and ≤46%, respectively, and higher for *Staphylococcus aureus*. There was a trend towards higher rates of AMR in patients with poorer lung function and greater incidence of previous antibiotic exposure and hospitalisation. The impact of AMR on mortality was unclear. Data regarding antimicrobial susceptibility testing techniques and the impact of other risk factors or consequences of AMR were variable or not reported. This is the first review to systematically unify data regarding AMR in COPD. AMR is relatively common and strategies to optimise antibiotic use could be valuable to prevent the currently under-investigated potential adverse consequences of AMR.

https://www.tandfonline.com/doi/full/10.1080/15412555.2021.2000957

Blood eosinophils have been proposed as a surrogate biomarker of airway eosinophilia that can be used for treatment decisions in patients with COPD, mainly for the identification of candidates for the initiation or withdrawal of therapy with inhaled corticosteroids, as well as for the identification of patients at future risk of exacerbations. In this manuscript we review the recent literature on blood eosinophils in the management of patients with COPD, in an attempt to answer the major questions that are relevant for the practicing clinician. A growing body of evidence suggests that eosinophilic COPD may constitute a separate phenotype of the disease with distinct clinical features and blood eosinophils may represent a potential candidate surrogate marker for specific COPD patients. Several points still need to be clarified, including the role of eosinophils for the identification of candidates for future COPD therapies, yet blood eosinophils plausibly represent the most dependable and promising biomarker for the precision management of COPD today.

https://www.tandfonline.com/doi/abs/10.1080/15412555.2021.1985989

Mortality and Exacerbation Risk by Body Mass Index in Patients with COPD in TIOSPIR and UPLIFT

SAUDI COPD GROUP

Rationale: There is an association between body mass index (BMI) and mortality in chronic obstructive pulmonary disease (COPD), with underweight individuals having higher mortality risk. Mortality and exacerbation risks among individuals with higher BMI are unclear.

Objectives: To examine the relationship between BMI and adverse outcomes in COPD.

Methods: This post hoc analysis included data from TIOSPIR (Tiotropium Safety and Performance in Respimat) (N = 17,116) and tiotropium-treated patients in UPLIFT (Understanding Potential Long-term Impacts on Function with Tiotropium) (N = 2,986). BMI classes (underweight [BMI < 20 kg/m^2], normal weight [BMI 20 to <25 kg/m^2], overweight [BMI 25 to <30 kg/m^2],obesity class I [BMI 30 to <35 kg/m^2], obesity class II [BMI 35 to <40 kg/m^2], and obesity class III [BMI ≥ 40 kg/m^2]) were examined for adjusted associations with mortality, exacerbation, and nonfatal cardiovascular event risk using over 50,000 patient-years of cumulative follow-up data. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox regression models.

Results: In TIOSPIR, obesity prevalence was 22%, overweight 32%, and underweight 12%. The proportion of females was highest in obesity classes II and III. Overweight and obese participants had better baseline lung function versus other BMI classes; underweight participants were more likely to be current smokers. Underweight participants had a significantly higher risk of death (HR, 1.88; 95% CI, 1.62–2.20; P < 0.0001) and severe exacerbations (HR, 1.31; 95% CI, 1.16–1.47; P < 0.0001) versus normal-weight participants; however, overweight and obese participants were at lower to no additional risk. Results from UPLIFT were similar to TIOSPIR.

Conclusions: These results suggest that there is a strong association between body weight, COPD events, and risk of death. A holistic management approach taking into account respiratory and cardiovascular risk factors and nutritional status is needed to improve the general well-being of patients with COPD.

https://www.atsjournals.org/doi/full/10.1513/AnnalsATS.202006-722OC

Development of a simple screening tool for opportunistic COPD case finding in primary care in Latin America:

SAUDI COPD GROUP

The PUMA study (patients scored 5 points or more should request Spirometry)

PUMA SCORE

Please check with an X:	Score assigned
1. Female ◯ male ◯	F (0) M (1) ☐
2. Enter your age in ☐	40-49 years (0) ☐ 50-59 years (1) ☐ 60+ years (2) ☐
3. Smoking:	
a. Have you ever smoked in your life? NO ☐	<20 pack-year (0) ☐ 20-30 pack-year (1) ☐ >30 pack-year (2) ☐

(If the interviewee smoked less than 20 packets in a lifetime or less than 1 cigarette a day in one year, check NO)

(Calculation of pack-year: Years of smoking X number of cigarettes per day/20)

Average cigarettes per day ☐ Number of years smoking ☐

4. Do you feel short of breath at some point when you walk faster on flat ground or a small incline?	NO (0) YES (1) ☐
5. Do you usually have phlegm coming from your lungs or difficulty expelling phlegm when not suffering from a cold?	NO (0) YES (1) ☐
6. Do you usually have a cough when not suffering from a cold?	NO (0) YES (1) ☐
7. Have you ever been asked by a doctor or other health professional to blow into a device (called a spirometer or peak flow meter) to know your lung function?	NO (0) YES (1) ☐
	Total score ☐

Interpretation: >5 points: request spirometry.

https://onlinelibrary.wiley.com/doi/epdf/10.1111/resp.12834

Saudi COPD group Panel

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Activities:

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Meeting:

The 1st Saudi COPD symposium June 2022