LIBRA JOURNAL CLUB
15-22 JANUARY 2023

COPD

Gene expression profiles in mesenchymal stromal cells from bone marrow, adipose tissue and lung tissue of COPD patients and controls

Dennis Kruk [# 1 2], Anna C Y Yeung [# 3 4], Alen Faiz [3], Nick H T Ten Hacken [2 5], Wim Timens [1 2], Toin H van Kuppevelt [6], Willeke Daamen [6], Danique Hof [6], Martin C Harmsen [1], Mauricio Rojas [7], Irene H Heijink [8 9 10]

Affiliations expand

- PMID: 36681830

- DOI: 10.1186/s12931-023-02314-8

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is characterized by irreversible lung tissue damage. Novel regenerative strategies are urgently awaited. Cultured mesenchymal stem/stromal cells (MSCs) have shown promising results in experimental models of COPD, but differences between sources may impact on their potential use in therapeutic strategies in patients.

Aim: To assess the transcriptome of lung-derived MSCs (LMSCs), bone marrow-derived MSCs (BM-MSC) and adipose-derived MSCs (AD-MSCs) from COPD patients and non-COPD controls.

Methods: We studied differences in gene expression profiles between the MSC-subtypes, as well as between COPD and control using RNA sequencing (RNA-seq).

Results: We show that besides heterogeneity between donors, MSCs from different sources have strongly divergent gene signatures. The growth factors FGF10 and HGF were predominantly expressed in LMSCs. MSCs from all sources displayed altered expression profiles in COPD, with most pronounced significantly up- and downregulated genes in MSCs from adipose tissue. Pathway analysis revealed that the most differentially expressed genes in COPD-derived AD-MSCs are involved in extracellular matrix (ECM) binding and expression. In LMSCs, the gene that differed most strongly between COPD and control was CSGALNACT1, an ECM modulating gene.

Conclusion: Autologous MSCs from COPD patients display abnormalities with respect to their transcriptome, which were surprisingly most profound in MSCs from extrapulmonary sources. LMSCs may be optimally equipped for lung tissue repair because of the expression of specific growth factor genes.

Keywords: Adipose tissue; Bone marrow; COPD pathology; Lung tissue; Mesenchymal stromal cells; Transcriptomics.

- [36 references]

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Improvements in health status with revefenacin, a once-daily, nebulized, long-acting muscarinic antagonist for chronic obstructive pulmonary disease

[James F Donohue](#) [1], [Gary T Ferguson](#) [2], [Jill A Ohar](#) [3], [David A Lombardi](#) [4], [Roslyn F Schneider](#) [5], [Karmon Johnson](#) [6]

Affiliations expand

- PMID: 36681255

- DOI: [10.1016/j.rmed.2023.107123](#)

Abstract

Background: Replicate 12-week phase 3 trials (0126 and 0127) of once-daily nebulized revefenacin 175 μg vs placebo demonstrated significant bronchodilation and improvements in health status in patients with moderate to very severe chronic obstructive pulmonary disease (COPD). This post hoc analysis evaluated improvement in patient-reported outcomes (PROs), including the St. George's Respiratory Questionnaire (SGRQ), COPD Assessment Test (CAT), and Clinical COPD Questionnaire (CCQ) in both women and men.

Methods: Participants were pooled from the two 12-week studies (411 [51%] women and 401 [49%] men). Changes in PROs were assessed overall and separately in men and women.

Results: Revefenacin improved SGRQ and CAT total scores from baseline in both studies; improvement in CCQ total score reached significance only in 0126. In pooled data, a greater proportion of patients achieved clinically meaningful response in SGRQ score (≥4-unit decrease from baseline) with revefenacin vs placebo (odds ratio, 1.5; 95% confidence interval, 1.1-2.1; P = 0.012). Clinically meaningful responses were also seen in CAT (≥2-unit

decrease from baseline) and CCQ (≥0.4-unit decrease from baseline) scores with revefenacin vs placebo. When stratified by sex, improvements from baseline in SGRQ, CAT, and CCQ scores following revefenacin vs placebo reached statistical significance only in women.

Conclusions: Maintenance treatment with revefenacin improved health status in patients with moderate to very severe COPD; however, the effect was more pronounced for women than men.

Clinicaltrials: GOV: [NCT02459080](); [NCT02512510]().

Keywords: COPD; COPD Assessment test; Clinical COPD Questionnaire; Patient-reported outcomes; Revefenacin; St. George's respiratory questionnaire.

Conflict of interest statement

Declaration of competing interest JFD is a consultant and advisory committee member for Theravance Biopharma US, Inc.; Sunovion Pharmaceuticals; and Mylan, a Viatris company. GTF is a consultant and speaker for and received financial support from Theravance Biopharma US, Inc., and Mylan, a Viatris company. JAO has served on advisory boards for AstraZeneca, Boehringer Ingelheim, GSK, Mylan Inc., Reckitt Benckiser, Sunovion Pharmaceuticals, and Theravance Biopharma US, Inc.DAL was a contract employee of Theravance Biopharma US, Inc., at the time of this study. RFS is an employee of BioMarin Pharmaceuticals, Inc.; has received consulting fees from GSK, Merck, and BreathResearch; and has received salary from Pfizer and from Theravance Biopharma US, where she was employed when these analyses were done. KJ is an employee of Theravance Biopharma US, Inc.

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☐ 3

J Crit Care

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[A randomized controlled trial comparing non-invasive ventilation delivered using neurally adjusted ventilator assist (NAVA) or adaptive support ventilation (ASV) in patients with acute exacerbation of chronic obstructive pulmonary disease](#)

[Bharath A Chhabria](#)[1], [Kuruswamy Thurai Prasad](#)[1], [Sahajal Dhooria](#)[1], [Valliappan Muthu](#)[1], [Ashutosh Nath Aggarwal](#)[1], [Ritesh Agarwal](#)[1], [Raghava Rao Gandra](#)[1], [Inderpaul Singh Sehgal](#)[2]

Affiliations expand

Abstract

Purpose: No study has compared neurally adjusted ventilator assist (NAVA) with adaptive support ventilation (ASV) during non-invasive ventilation (NIV) in subjects with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Materials and methods: In this randomized controlled trial, we compared NAVA-NIV with ASV-NIV for delivering NIV in consecutive subjects with AECOPD. The primary outcome was NIV failure rate (invasive mechanical ventilation). The key secondary outcomes were number of NIV manipulations, asynchrony index, and 90-day mortality.

Results: We enrolled 76 subjects (NAVA-NIV, n = 36, ASV-NIV, n = 40; 74% males) with a mean ± SD age of 61.4 ± 8.2 years. We found no difference in NIV failure rates between the two arms (NAVA-NIV vs. ASV-NIV; 8/36 [22.2%] vs. 8/40 [20%]; p = 0.83). The median physician manipulations for NIV were significantly less in the ASV-NIV arm than in the NAVA-NIV arm (2 [0.8-4] vs. 3 [2-5]; p= 0.014) during the initial 24-h. We found no

difference in median asynchrony index (NAVA-NIV vs. ASV-NIV, 16.6% vs. 16.4%, p = 0.5) and 90-day mortality (22.2% vs. 17.5%, p = 0.67).

Conclusion: The use of NAVA-NIV was not superior to ASV-NIV in reducing NIV failure rates in AECOPD. Both NAVA-NIV and ASV-NIV had similar asynchrony index and 90-day mortality.

Trial registry: www.

Clinicaltrials: gov (NCT04414891).

Keywords: BIPAP; Mechanical ventilation; NAVA; NIV; PSV; Respiratory failure.

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Review

Alarmins and MicroRNAs, a New Axis in the Genesis of Respiratory Diseases: Possible Therapeutic Implications

Alessandro Allegra [1], Giuseppe Murdaca [2], Luca Gammeri [3], Roberta Ettari [4], Sebastiano Gangemi [3]

Abstract

It is well ascertained that airway inflammation has a key role in the genesis of numerous respiratory pathologies, including asthma, chronic obstructive pulmonary disease, and acute respiratory distress syndrome. Pulmonary tissue inflammation and anti-inflammatory responses implicate an intricate relationship between local and infiltrating immune cells and structural pulmonary cells. Alarmins are endogenic proteins discharged after cell injury in the extracellular microenvironment. The purpose of our review is to highlight the alterations in respiratory diseases involving some alarmins, such as high mobility group box 1 (HMGB1) and interleukin (IL)-33, and their inter-relationships and relationships with genetic non-coding material, such as microRNAs. The role played by these alarmins in some pathophysiological processes confirms the existence of an axis composed of HMGB1 and IL-33. These alarmins have been implicated in ferroptosis, the onset of type 2 inflammation and airway alterations. Moreover, both factors can act on non-coding genetic material capable of modifying respiratory function. Finally, we present an outline of alarmins and RNA-based therapeutics that have been proposed to treat respiratory pathologies.

Keywords: acute respiratory distress syndrome; alarmins; asthma; epigenetics; high mobility group box 1; immune response; inflammation; interleukin-33; microRNAs; respiratory diseases.

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Pharmacoeconomics

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Population-Based Screening Using Low-Dose Chest Computed Tomography: A Systematic Review of Health Economic Evaluations

Carina M Behr [1], Martijn J Oude Wolcherink [1], Maarten J IJzerman [1 2 3], Rozemarijn Vliegenthart [4], Hendrik Koffijberg [5]

Affiliations expand

- PMID: 36670332

- DOI: 10.1007/s40273-022-01238-3

Abstract

Background: Chest low-dose computed tomography (LDCT) is a promising technology for population-based screening because it is non-invasive, relatively inexpensive, associated with low radiation and highly sensitive to lung cancer. To improve the cost-effectiveness of lung cancer screening, simultaneous screening for other diseases could be considered. This systematic review was conducted to analyse studies that published evidence on the cost-effectiveness of chest LDCT screening programs for different diseases.

Methods: Scopus and PubMed were searched for English publications (1 January 2011-22 July 2022) using search terms related to screening, computed tomography and cost-effectiveness. An additional search specifically searched for the cost-effectiveness of screening for lung cancer, chronic obstructive pulmonary disease or cardiovascular disease. Included publications should present a full health economic evaluation of population screening with chest LDCT. The extracted data included the disease screened for, model type, country context of screening, inclusion of comorbidities or incidental findings, incremental costs, incremental effects and the resulting cost-effectiveness ratio amongst others. Reporting quality was assessed using the 2022 Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.

Results: The search yielded 1799 unique papers, of which 43 were included. Most papers focused on lung cancer screening (n = 40), and three were on coronary calcium scoring.

Microsimulation was the most commonly applied modelling type (n = 16), followed by life table analysis (n = 10) and Markov cohort models (n = 10). Studies reflected the healthcare context of the US (n = 15), Canada (n = 4), the UK (n = 3) and 13 other countries. The reported incremental cost-effectiveness ratio ranged from US$10,000 to US$90,000/quality-adjusted life year (QALY) for lung cancer screening compared to no screening and was US$15,900/QALY-US$45,300/QALY for coronary calcium scoring compared to no screening.

Discussion: Almost all health economic evaluations of LDCT screening focused on lung cancer. Literature regarding the health economic benefits of simultaneous LDCT screening for multiple diseases is absent. Most studies suggest LDCT screening is cost-effective for current and former smokers aged 55-74 with a minimum of 30 pack-years of smoking history. Consequently, more evidence on LDCT is needed to support further cost-effectiveness analyses. Preferably evidence on simultaneous screening for multiple diseases is needed, but alternatively, on single-disease screening.

Registration of systematic review: Prospective Register of Ongoing Systematic Reviews registration CRD42021290228 can be accessed https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=290228 .

- 67 references

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[Out-of-Hospital Presentation and Management of Asthma and Chronic Obstructive Pulmonary Disease Exacerbations in the United States: A Nationwide Retrospective Cohort Study](#)

[Gregory A Peters](#) [1], [Rebecca E Cash](#) [2], [Scott A Goldberg](#) [3], [Alexander J Ordoobadi](#) [4], [Carlos A Camargo Jr](#) [5]

Affiliations expand

Abstract

Study objective: To describe the demographic, clinical, and emergency medical service (EMS) response characteristics associated with EMS activations for asthma and chronic obstructive pulmonary disease (COPD) exacerbations in the US.

Methods: Using a nationwide set of out-of-hospital patient care report data from 2018 to 2019, we analyzed 9-1-1 EMS activations where asthma/COPD exacerbation was indicated by symptom, impression, or treatment provided. We excluded patients with ages less than 2 years or unknown, nonemergency transports, and encounters with any indication of anaphylaxis. Demographic, clinical, and EMS response characteristics were described for pediatric and adult patients with asthma/COPD exacerbations.

Results: A total of 1,336,988 asthma/COPD exacerbations were included, comprising 5% of qualifying 9-1-1 scene activations from 2018 to 2019. Most patients were adults (96%). Most adult patients were female (55%), whereas most pediatric patients were male (58%). Most activations occurred in urban settings (82%), particularly in pediatric patients (90%). Most asthma/COPD exacerbations were managed by advanced life support units (94%). Inhaled bronchodilators and systemic corticosteroid therapy were administered to 75% and 14% of all patients, respectively. Adults more often had oxygen saturation <92% (43% vs 20% of pediatric patients) and were more often treated with assisted ventilation (9% vs 1%).

Conclusion: In this large nationwide sample of 9-1-1 activations treated and transported by EMS, 5% were for asthma/COPD exacerbation. Future work should focus on evidence-based standardization of EMS protocols and practice for asthma/COPD exacerbations to improve the quality of EMS care.

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Principal stratification analysis to determine health benefit of indoor air pollution reduction in a randomized environmental intervention in COPD: Results from the CLEAN AIR study

Han Woo [1], Kirsten Koehler [2], Nirupama Putcha [3], Wendy Lorizio [3], Meredith McCormack [4], Roger Peng [5], Nadia N Hansel [4]

Affiliations expand

Abstract

Background: Indoor air quality represents a modifiable exposure to Chronic Obstructive Pulmonary Disease (COPD) health. In a randomized controlled trial (CLEAN AIR study), air cleaner assignment had causal effect in improving COPD outcomes. It is unclear, however, what is the treatment effect among those for whom intervention reduced air pollution and whether it was reduction in fine particulate matter ($PM_{2.5}$) or nitrogen dioxide (NO_2) that contributed to such improvement. Because pollution is a posttreatment variable, treatment effect cannot be assessed while controlling for pollution using intention-to-treat (ITT) analysis.

Objective: Using principal stratification method, we assess indoor pollutants as the intermediate variable, and determine the causal effect of reducing indoor air pollution on COPD health.

Method: In randomized controlled trial, former smokers with COPD received either active or placebo HEPA air cleaners and were followed for 6 months. Saint George's Respiratory Questionnaire (SGRQ) was the primary outcome and secondary measures included SGRQ subscales, COPD assessment test (CAT), dyspnea (mMRC), and breathlessness, cough, and sputum scale (BCSS). Indoor $PM_{2.5}$ and NO_2 were measured. Principal stratification analysis was performed to assess the treatment effect while controlling for pollution reduction.

Results: Among those showing at least 40 % $PM_{2.5}$ reduction through air cleaners, the intervention showed improvement in respiratory symptoms for the active (vs. placebo), and the size of treatment effect shown for this subgroup was larger than that for the overall sample. In this subgroup, those with active air cleaners (vs. placebo) showed 7.7 points better SGRQ (95%CI: -14.3, -1.1), better CAT (β = -5.5; 95%CI: -9.8, -1.2), mMRC (β = -0.6; 95%CI: -1.1, -0.1), and BCSS (β = -1.8; 95%CI: -3.0, -0.5). Among those showing at least 40 % NO_2 reduction through air cleaners, there was no intervention difference in outcomes.

Conclusion: Air cleaners caused clinically significant improvement in respiratory health for individuals with COPD through reduction in indoor $PM_{2.5}$.

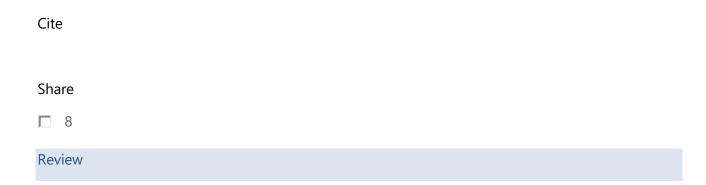**Trial registration:** ClinicalTrials.gov: [NCT02236858](NCT02236858).

Keywords: Air cleaners; COPD; Environment; Particulate matter; Principal stratification; Randomized controlled trial.

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Cerebral oxygenation during cardiopulmonary exercise testing in cardiorespiratory diseases: A systematic review

[Gabriela Aguiar Mesquita Galdino](#) [1], [Patrícia Rehder-Santos](#) [1], [Stephanie Nogueira Linares](#) [1], [Thomas Beltrame](#) [2], [Aparecida Maria Catai](#) [3]

Affiliations expand

- PMID: 36669443

- DOI: [10.1016/j.hrtlng.2023.01.004](#)

Abstract

Background: Cardiopulmonary exercise testing (CPET) is the gold standard for analyzing cardiorespiratory fitness and integrating physiological responses. However, the presence of chronic diseases may compromise cerebral hemodynamic responses during CPET. In addition, the acute response of cerebral oxygenation during incremental CPET may identify abnormal behavior and ensure greater safety for patients with cardiovascular, respiratory, and metabolic diseases.

Objective: To summarize the cerebral oxygenation acute response during CPET of patients with cardiovascular, metabolic, or respiratory diseases.

Methods: From inception to 23rd September 2022, five databases (PubMed, SCOPUS, Web of Science, Embase and CINAHAL) were searched for cross-sectional studies performing incremental CPET and measuring the cerebral oxygenation acute response in cardiovascular, metabolic, or respiratory diseases compared with healthy individuals. The Downs and Black tool assessed the risk of bias of the studies.

Results: We included seven studies with 428 participants (305 men and 123 women), aged 43 to 70 years. Of these, 101 had heart failure NYHA II and III; 77 idiopathic dilated cardiomyopathy; 33 valvular disease; 25 coronary heart disease; 22 pulmonary arterial hypertension; 15 had severe obstructive sleep apnea (OSA) and 166 were apparently healthy. There was no eligible article with metabolic disease. There was a lower magnitude increase in cerebral oxygenation of cardiovascular patients compared with the healthy individuals during the CPET. Furthermore, pulmonary arterial hypertension patients presented increased cerebral oxygen extraction, differently to those with severe OSA.

Conclusion: Considering the heterogeneity of the included studies, patients with cardiovascular disease may suffer from reduced cerebral oxygen supply, and individuals with OSA presented lower brain oxygen extraction during the CPET. Future studies should aim for strategies to improve cerebral oxygenation to ensure greater safety at CPET of cardiovascular and OSA patients. An acute response pattern for metabolic and other respiratory diseases was not established.

Keywords: Exercise testing; Heart disease; Near infrared spectroscopy; Oxygenation; Respiratory disease; Systematic review.

Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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The clinical spectrum of aspergillosis in chronic obstructive pulmonary disease

Akaninyene Otu [1], Chris Kosmidis [2], Alexander G Mathioudakis [3][4], Chibuike Ibe [5], David W Denning [6]

Affiliations expand

- PMID: 36662439

- DOI: 10.1007/s15010-022-01960-2

Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. In this review, we present the clinical spectrum and pathogenesis of syndromes caused by Aspergillus in COPD namely invasive aspergillosis (IA), community-acquired Aspergillus pneumonia, chronic pulmonary Aspergillosis and Aspergillus sensitisation. Some of these entities are clearly linked to COPD, while others may coexist, but are less clearly liked directly to COPD. We discuss current uncertainties as these pertain to IA in COPD cohorts and explore areas for future research in this field.

Keywords: Aspergillosis; Bronchiectasis; Chronic pulmonary disease.

- 157 references

SUPPLEMENTARY INFO

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Cough Assessment and Management in Pulmonary Rehabilitation– A Canadian Survey

Ana Maria Ilicic [1], Dina Brooks [1][2][3], Michelle Kho [1][4][5], Roger Goldstein [2][3], Ana Oliveira [1][2][6][7]

Affiliations expand

- PMID: 36656707

- DOI: 10.1080/15412555.2022.2141622

Abstract

Pulmonary rehabilitation is a cornerstone intervention for controlling respiratory symptoms in people with chronic respiratory diseases. Chronic cough affects up to 90% of people with chronic respiratory diseases, however, it is currently unknown whether chronic cough is assessed and/or managed in pulmonary rehabilitation. This study aimed to determine if and how chronic cough is assessed and managed in pulmonary rehabilitation. This was a cross-sectional study. Pulmonary rehabilitation programs in Canada were identified *via* online websites. A representative from each program was invited to complete an online survey including the following topics: program demographics, assessment and management practices, and barriers and facilitators. Of 133 programs contacted, 31 returned a completed survey (23% response rate). Approximately half (52%) of respondents reported enrolling patients with chronic cough. Of those, 45% reported

assessing and 62% reported intervening in chronic cough. Inadequate knowledge of assessment and management techniques was commonly identified to be a barrier and increased education was suggested as a possible facilitator. Based on pulmonary rehabilitation programs that responded to our survey, chronic cough is a prevalent symptom; however, it is scarcely assessed and managed. A need for structured education and the use of standardised strategies were reported as facilitators to the assessment and management of chronic cough in pulmonary rehabilitation.

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Short- and Long-Term Impact of Prior Chronic Obstructive Pulmonary Disease Exacerbations on Healthcare Resource Utilization and Related Costs: An Observational Study (SHERLOCK)

Enrico de Nigris [1], John Haughney [2], Amanda J Lee [3], Mintu Nath [3], Hana Müllerová [4], Ulf Holmgren [5], Bo Ding [5]

Affiliations expand

Abstract

The observational retrospective cohort Study on HEalthcare Resource utiLization (HCRU) related to exacerbatiOns in patients with COPD (SHERLOCK; D5980R00014) evaluated exacerbation-related HCRU and costs using the U.K. National Health Service Greater Glasgow and Clyde Health Board data. Patients (≥40 years) with COPD were stratified by exacerbations one year before the index date: Group A (none), B (1 moderate), C (1 severe) and D (≥2 moderate and/or severe). All-cause and COPD-related HCRU and costs were assessed over 36 months. Adjusted rate ratios (RRs) or relative costs versus Group A were estimated using generalized linear models with appropriate distributions and link functions. The study included 22 462 patients (Group A, n = 7788; B, n = 5151; C, n = 250 and D, n = 9273). At 12 months, RRs (95% CI) versus Group A for all-cause and COPD-related HCRU, respectively, were highest in Groups C (1.28 [1.18, 1.39] and 1.18 [1.09, 1.29]) and D (1.26 [1.23, 1.28] and 1.29 [1.26, 1.31]). General practitioner and outpatient visits, and general ward stays/days accounted for the greatest COPD-related HCRU. All-cause and COPD-related relative costs (95% CI) versus Group A at 12 months, respectively, were 1.03 (0.94, 1.12) and 1.06 (0.99, 1.13) in Group B; 1.47 (1.07, 2.01) and 1.54 (1.20, 1.97) in Group C; 1.47 (1.36, 1.58) and 1.63 (1.54, 1.73) in Group D. Increased HCRU and costs in patients with exacerbation histories persisted at 36 months, demonstrating the sustained impact of exacerbations. The study suggests the importance of management and prevention of exacerbations through intervention optimization and budgeting by payers for exacerbation-related costs.

Keywords: Chronic obstructive pulmonary disease; exacerbation history; exacerbation severity; healthcare costs; healthcare resource utilization.

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COPD

Association between Galectin-13 Expression and Eosinophilic Airway Inflammation in Chronic Obstructive Pulmonary Disease

Lingling Yi [1][2], Yuchen Feng [1][2], Dian Chen [1][2], Yanling Jin [3], Shuchen Zhang [4]

Affiliations expand

Abstract

Chronic obstructive pulmonary disease (COPD) and asthma are chronic inflammatory diseases of the airways. Galectin-13 has recently been forwarded as a biomarker for airway eosinophilic inflammation in asthma. However, the association between galectin-13 and COPD remains unknown. To examine the changes in galectin-13 expression in acute exacerbations of COPD (AECOPD) and the stable phase of COPD and unveil the association between galectin-13 expression and eosinophilic inflammation in COPD, we measured plasma galectin-13 expression in different phases of COPD patients (n = 60, 44 AECOPD patients, and 16 stable COPD patients) and healthy controls (n = 15). Plasma levels of galectin-13 in 60 COPD patients were further analyzed and compared to systemic inflammation, airway eosinophilic inflammation, and lung function. The plasma galectin-13 level was markedly increased in subjects with AECOPD compared to stable COPD patients and healthy controls. Plasma galectin-13 levels in COPD subjects were positively correlated with serum CRP (r_s = 0.46, p = 0.0003), peripheral blood eosinophilia count (r_s = 0.57, $p<0.0001$), and FeNO (r_s = 0.46, p = 0.0002). In addition, the level of galectin-13 was negatively correlated with FEV_1 (r_s = -0.43, p = 0.0001), FEV_1 pred (%) (r_s = -0.544, $p<0.0001$), as well as FEV_1/FVC (r_s = -0.46, $p<0.0001$). Multiple linear regression analysis suggested that plasma galectin-13 levels were affected by FEV_1 pred (%), peripheral blood eosinophilia count, and FeNO. We concluded that galectin-13 levels were increased in COPD patients, and elevated galectin-13 expressions related to airway

eosinophilic inflammation. Galectin-13 may facilitate the identification of COPD endotypes and may become a potential therapeutic target.

Keywords: CRP; chronic obstructive pulmonary disease; eosinophilic inflammation; galectin-13.

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Nighttime continuous contactless smartphone-based cough monitoring for the ward: A validation study

Filipe Barata [1], David Cleres [1], Peter Tinschert [1 2], Iris Shih [1 2], Frank Rassouli [3], Maximilian Boesch [3], Martin Brutsche [3], Elgar Fleisch [1 4]

Affiliations expand

Free article

Abstract

Background: Clinical deterioration can go unnoticed in hospital wards for hours. Mobile technologies such as wearables and smartphones enable automated, continuous, non-invasive ward monitoring and allow the detection of subtle changes in vital signs. Cough holds great potential for monitoring through mobile technologies on the ward as it is not only a symptom of prevalent respiratory diseases such as asthma, lung cancer, and COVID-19 but also a predictor of acute health deterioration. In past decades, many efforts have been made to develop an automatic cough counting tool. To date, however, there is neither a standardized, sufficiently validated method nor a scalable cough monitor that can be deployed on a consumer-centric device that reports cough counts continuously. These shortcomings limit the tracking of coughing and, consequently, hinder the monitoring of disease progression in prevalent respiratory diseases such as asthma, chronic obstructive pulmonary disease, and COVID-19 in the ward.

Objective: This exploratory study involves the validation of an automated smartphone-based monitoring system for continuous cough counting in two different modes in the ward. Unlike previous studies that focused on evaluating cough detection models on unseen data, the focus of this work is to validate a holistic smartphone-based cough detection system operating in near real-time.

Methods: Automated cough counts are measured consistently on-device and on-computer, and compared with cough and non-cough sounds counted manually over eight hours long nocturnal recordings in nine patients with pneumonia in the ward. The proposed cough detection system consists primarily of an Android app running on a smartphone that detects coughs and records sounds, and secondarily of a backend that continuously receives the cough detection information and displays the hourly cough counts. Cough detection is based on an ensemble Convolutional Neural Network developed and trained on asthmatic cough data.

Results: In this validation study, a total of 72 hours of recording from nine participants with pneumonia, four of whom were infected with SARS-CoV-2, were analyzed. All recordings were subjected to manual analysis by two blinded raters. The proposed system yielded sensitivity and specificity of 72% and 99% on-device and 82% and 99% on-computer, respectively, for detecting coughs. The mean difference between the automated and human rater cough counts were -1.0, CI 95% [-12.3, 10.2] and -0.9, CI 95% [-6.5, 4.8] coughs per hour within-subject for the on-device and on-computer mode, respectively.

Conclusions: The proposed system thus represents a smartphone cough counter that can be used for continuous hourly assessment of cough frequency in the ward.

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JMIR Publications Preprint

Association between cadmium exposure and pulmonary function reduction: Potential mediating role of telomere attrition in chronic obstructive pulmonary disease patients

Bian-Bian Lv [1], Chun-Lan Yang [2], Zhu-Xia Tan [3], Ling Zheng [3], Meng-Die Li [3], Ya-Lin Jiang [4], Ling Liu [5], Min-Min Tang [3], Dong-Xu Hua [3], Jin Yang [3], De-Xiang Xu [6], Hui Zhao [7], Lin Fu [8]

Affiliations expand

- PMID: 36652742

- DOI: 10.1016/j.ecoenv.2023.114548

Abstract

Background: Environmental cadmium (Cd) exposure is linked to pulmonary function injury in the general population. But, the association between blood Cd concentration and pulmonary function has not been investigated thoroughly in chronic obstructive pulmonary disease (COPD) patients, and the potential mechanisms are unclear.

Methods: All eligible 789 COPD patients were enrolled from Anhui COPD cohort. Blood specimens and clinical information were collected. Pulmonary function test was conducted. The subunit of telomerase, telomerase reverse transcriptase (TERT), was determined through enzyme linked immunosorbent assay (ELISA). Blood Cd was measured via inductively coupled-mass spectrometer (ICP-MS).

Results: Blood Cd was negatively and dose-dependently associated with pulmonary function. Each 1-unit increase of blood Cd was associated with 0.861 L decline in FVC, 0.648 L decline in FEV1, 5.938 % decline in FEV1/FVC %, and 22.098 % decline in FEV1 % among COPD patients, respectively. Age, current-smoking, self-cooking and higher smoking amount aggravated Cd-evoked pulmonary function decrease. Additionally, there was an inversely dose-response association between Cd concentration and TERT in COPD patients. Elevated TERT obviously mediated 29.53 %, 37.50 % and 19.48 % of Cd-evoked FVC, FEV1, and FEV1 % declines in COPD patients, respectively.

Conclusion: Blood Cd concentration is strongly associated with the decline of pulmonary function and telomerase activity among COPD patients. Telomere attrition partially mediates Cd-induced pulmonary function decline, suggesting an underlying mechanistic role of telomere attrition in pulmonary function decline from Cd exposure in COPD patients.

Keywords: Association; COPD; Cadmium; Pulmonary function; Telomerase.

Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Comparative Study

Survival and health care costs after inpatient elective surgery: comparison of patients with and without chronic obstructive pulmonary disease

Ashwin Sankar [1], Kevin Thorpe [2], Daniel I McIsaac [2], Jin Luo [2], Duminda N Wijeysundera [2], Andrea S Gershon [2]

Affiliations expand

- PMID: 36649951

- PMCID: PMC9851642

- DOI: 10.1503/cmaj.220733

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is common among surgical patients, and patients with COPD have higher risk for complications and death within 30 days after surgery. We sought to describe the longer-term postoperative survival and costs of patients with COPD compared with those without COPD within 1 year after inpatient elective surgery.

Methods: In this retrospective population-based cohort study, we used linked health administrative databases to identify all patients undergoing inpatient elective surgery in Ontario, Canada, from 2005 to 2019. We ascertained COPD status using validated definitions. We followed participants for 1 year after surgery to evaluate survival and costs to the health system. We quantified the association of COPD with survival (Cox

proportional hazards models) and costs (linear regression model with log-transformed costs) with partial adjustment (for sociodemographic factors and procedure type) and full adjustment (also adjusting for comorbidities). We assessed for effect modification by frailty, cancer and procedure type.

Results: We included 932 616 patients, of whom 170 482 (18%) had COPD. With respect to association with risk of death, COPD had a partially adjusted hazard ratio (HR) of 1.61 (95% confidence interval [CI] 1.58-1.64), and a fully adjusted HR of 1.26 (95% CI 1.24-1.29). With respect to impact on health system costs, COPD was associated with a partially adjusted relative increase of 13.1% (95% CI 12.7%-13.4%), and an increase of 4.6% (95% CI 4.3%-5.0%) with full adjustment. Frailty, cancer and procedure type (such as orthopedic and lower abdominal surgery) modified the association between COPD and outcomes.

Interpretation: Patients with COPD have decreased survival and increased costs in the year after surgery. Frailty, cancer and the type of surgical procedure modified associations between COPD and outcomes, and must be considered when risk-stratifying surgical patients with COPD.

Conflict of interest statement

- 46 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Interrelationships between tuberculosis and chronic obstructive pulmonary disease

Michael J Zavala[1], Greta L Becker, Robert J Blount

Affiliations expand

- PMID: 36647566

- DOI: 10.1097/MCP.0000000000000938

Abstract

Purpose of review: Our objective was to review the current literature regarding socioeconomic, environmental, clinical, and immunologic factors common to chronic obstructive pulmonary disease (COPD) and tuberculosis (TB).

Recent findings: Recent studies suggest that TB patients might be at increased risk for developing COPD. Conversely, additional prospective cohort studies have determined that COPD patients are at increased risk for active TB: a risk that appears to be partially mediated through inhaled corticosteroid use. Tobacco smoking, poverty, air pollution, and malnutrition are associated with COPD and TB. Vitamin D has been shown to prevent COPD exacerbations, but its use for preventing TB infection remains unclear. Surfactant deficiency, elevated matrix metalloproteinases, and toll-like receptor 4 polymorphisms play key roles in the pathogenesis of both diseases.

Summary: Recent studies have elucidated interrelationships between COPD and TB. Future research is needed to optimize clinical and public health approaches that could mitigate risk factors contributing to both diseases.

- <u>100 references</u>

Randomized Controlled Trial

Efficacy and safety of long-term use of a positive expiratory pressure device in chronic obstructive pulmonary disease patients, a randomized controlled trial

<u>Zhaoning Xu</u> [1], <u>Zhuo Han</u> [2], <u>Dedong Ma</u> [3]

Affiliations expand

Abstract

Background: Exercise intolerance is among the most common symptoms experienced by patients with chronic obstructive pulmonary disease (COPD), which is associated with lung dynamic hyperinflation (DH). There was evidence that positive expiratory pressure (PEP), which could be offered by less costly devices, could reduce DH. The purpose of this study was to evaluate the efficacy and safety of long-term domiciliary use of PEP device in subjects with COPD.

Methods: A randomized controlled trial was conducted and 25 Pre-COPD or mild-to-very severe subjects with COPD were randomized to intervention group (PEP device, PEP = 5 cmH_2O, n = 13) and control group (Sham-PEP device, PEP = 0 cmH_2O, n = 12). PEP device was a spring-loaded resistor face mask. Subjects were treated 4 h per day for a total of 2 months. Six-minute walk test (6MWT), pulmonary function, the Modified British Medical Research Council score, and partial pressure of end-tidal carbon dioxide were evaluated at baseline and after two months.

Results: The 6MWD (- 71.67 ± 8.70 m, P < 0.001), end-dyspnea (P = 0.002), and end-fatigue (P = 0.022) improved significantly in the intervention group when compared with the control group. All subjects in the intervention group reported that 4 h of daily use of the PEP device was well tolerated and accepted and there were no adverse events.

Conclusion: Regular daily use of PEP device is safe and may improve exercise capacity in subjects with COPD or pre-COPD. PEP device could be used as an add-on to pulmonary rehabilitation programs due to its efficacy, safety, and low cost.

Trial registration: The study was prospectively registered on ClinicalTrials.gov (NCT04742114).

Keywords: 6-min walk test; Chronic obstructive pulmonary disease; Dyspnea; Exercise capacity; Positive-pressure respiration.

Conflict of interest statement

The authors declare that they have no competing interests.

- 31 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated data, Grant supportexpand

Ageing and chronic obstructive pulmonary disease: interrelationships

Krishna Kakkera [1][2], William T Atchley [1][2], Maneetha Kodali [2], Thaddeus Bartter [1][2]

Affiliations expand

- PMID: 36644998

- DOI: 10.1097/MCP.0000000000000943

Abstract

Purpose of review: As life expectancy increases, the ageing population accrues an increasing burden of chronic conditions and functional compromise. Some conditions that lead to compromise are deemed part of 'natural ageing,' whereas others are considered to represent disease processes. Ageing ('a natural process') and chronic obstructive pulmonary disease ('a disease') share many common features, both pulmonary and systemic. At times, the pathways of injury are the same, and at times they are concurrent. In some cases, age and disease are separated not by the presence but by the severity of a

finding or condition. This brief review aims to compare some of the similarities between ageing and COPD and to compare/contrast mechanisms for each.

Recent findings: At the cellular level, the natural process of ageing includes multiple systemic and molecular mechanisms. COPD, though defined by progressive pulmonary compromise, can also be a systemic disease/process. It has become evident that specific senescence pathways like p-16 and the sirtuin family of proteins are implicated both in ageing and in COPD. Also common to both ageing and COPD are increased inflammatory markers, leucocyte response abnormalities, and DNA-level abnormalities.

Summary: The prevalence of COPD increases with increasing age. COPD contributes to the accrued burden of chronic disease and is a significant contributor to morbidity and mortality in this population. This review attempts to summarize some of similarities between ageing and COPD and their underlying mechanisms.

- 45 references

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Multicenter Study

Preoperative Comorbidities Associated With Early Mortality in Hip Fracture Patients: A Multicenter Study

Michael A McHugh [1], Jenna L Wilson, Nathaniel E Schaffer, Eric C Olsen, Aaron Perdue, Jaimo Ahn, Mark E Hake

Affiliations expand

Abstract

Objective: Multiple comorbidities in hip fracture patients are associated with increased mortality and complications. The goal of this study was to characterize the relationship between specific patient factors including comorbidities and outcomes in geriatric hip fractures, including length of stay, unplanned ICU admission, discharge disposition, complications, and mortality.

Methods: This is a retrospective review of a trauma database from five Level 1 and Level 2 trauma centers of patients with hip fractures of the femoral neck and intertrochanteric region who underwent treatment using hip pinning, hemiarthroplasty, total hip arthroplasty, cephalomedullary nailing, or dynamic hip screw fixation. Mortality was the primary outcome variable (including in-hospital mortality, 30-day mortality, 60-day mortality, and 90-day mortality). Secondary outcome variables included in-hospital adverse events, unplanned transfer to the ICU, postoperative length of stay, and discharge disposition. Regression analyses were used for evaluation of relationships between comorbidities as independent variables and primary and secondary outcomes as dependent variables.

Results: Two thousand three hundred patients were included. The mortality was 1.8%, 7.0%, 10.9%, and 14.1% for in-hospital, 30-day, 60-day, and 90-day mortality, respectively. Diabetes and cognitive impairment present on admission were associated with mortality at all-time intervals. COPD was the only comorbidity that signaled in-hospital adverse event with an odds ratio of 1.67 (P = 0.012). No patient factors, time to surgery, or comorbidities signaled unplanned ICU transfer. Patients with renal failure and COPD had longer hospital stays after surgery.

Conclusion: Geriatric hip fractures continue to have high short-term morbidity and mortality. Identifying patients with increased odds of early mortality and adverse events can help teams optimize care and outcomes. Patients with diabetes, cognitive impairment, renal failure, and COPD may benefit from continued and improved medical optimization during the perioperative period as well as being more closely managed by a medicine team without delaying time to the operating room.

- 41 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Impact of Adherence to Continuous Positive Airway Pressure on Outcomes in Obstructive Sleep Apnea Chronic Obstructive Pulmonary Disease Overlap Syndrome

[Johad Khoury](#) [1][2][3], [Fahed Hakim](#) [3][4]

Affiliations expand

- PMID: 36049224

- DOI: [10.1164/rccm.202207-1403LE](#)

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Respir Crit Care Med

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[Health Care Spending on Respiratory Diseases in the United States, 1996–2016](#)

[Kevin I Duan](#) [1][2], [Maxwell Birger](#) [3], [David H Au](#) [1][2], [Laura J Spece](#) [1][2], [Laura C Feemster](#) [1][2], [Joseph L Dieleman](#) [4]

Affiliations expand

Abstract

Rationale: Respiratory conditions account for a large proportion of health care spending in the United States. A full characterization of spending across multiple conditions and over time has not been performed. **Objectives:** To estimate health care spending in the United States for 11 respiratory conditions from 1996 to 2016, providing detailed trends and an evaluation of factors associated with spending growth. **Methods:** We extracted data from the Institute of Health Metrics and Evaluation's Disease Expenditure Project Database, producing annual estimates in spending for 38 age and sex groups, 7 types of care, and 3 payer types. We performed a decomposition analysis to estimate the change in spending associated with changes in each of five factors (population growth, population aging, disease prevalence, service usage, and service price and intensity). **Measurements and Main Results:** Total spending across all respiratory conditions in 2016 was $170.8 billion (95% confidence interval [CI], $164.2-179.2 billion), increasing by $71.7 billion (95% CI, $63.2-80.8 billion) from 1996. The respiratory conditions with the highest spending in 2016 were asthma and chronic obstructive pulmonary disease, contributing $35.5 billion (95% CI, $32.4-38.2 billion) and $34.3 billion (95% CI, $31.5-37.3 billion), respectively. Increasing service price and intensity were associated with 81.4% (95% CI, 70.3-93.0%) growth from 1996 to 2016. **Conclusions:** U.S. spending on respiratory conditions is high, particularly for chronic conditions like asthma and chronic obstructive pulmonary disease. Our findings suggest that service price and intensity, particularly for pharmaceuticals, should be a key focus of attention for policymakers seeking to reduce health care spending growth.

Keywords: health economics; health expenditures; health policy.

Comment in

- [How Much Does the United States Spend on Respiratory Diseases?](#)
Nurmagambetov TA.Am J Respir Crit Care Med. 2023 Jan 15;207(2):126-127. doi: 10.1164/rccm.202209-1696ED.PMID: 36155100 No abstract available.

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

AJRCCM
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Review

Steroid induced secondary immune deficiency

S Shahzad Mustafa [1]

Affiliations expand

- PMID: 36681272

- DOI: 10.1016/j.anai.2023.01.010

Abstract

Despite their widespread clinical use, oral corticosteroids (OCSs) are well known to be associated with a myriad of adverse effects, including immunosuppression. By inhibiting transcription factors and affecting leukocyte function, prolonged OCS use leads to significant CD4 lymphopenia, and also often leads to a decrease in serum IgG. Conversely, OCS use has minimal impact on circulating B cell, serum IgM, or serum IgA levels. Although there is a paucity of literature, individuals treated with prolonged OCS appear to typically maintain humoral response to various vaccinations despite hypogammaglobinemia, but this area warrant additional research, especially in the setting of the COVID-19 pandemic. Individuals treated with prolonged OCS use are most at risk for opportunistic infections, especially those with underlying malignancy and history of bone marrow transplant. Risk mitigation strategies to decrease infectious complication with OCS use include limiting the dose and duration of therapy, appropriately completing a full vaccination series, consideration for passive immunization, and prophylaxis against opportunistic infections.

Conflict of interest statement

Declaration of Competing of Interest S Shahzad Mustafa: speaker's bureau for Genentech, AstraZeneca, Regeneron, GSK, Aimmune, and CSL Behring.

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Out-of-Hospital Presentation and Management of Asthma and Chronic Obstructive Pulmonary Disease Exacerbations in the United States: A Nationwide Retrospective Cohort Study

Gregory A Peters [1], Rebecca E Cash [2], Scott A Goldberg [3], Alexander J Ordoobadi [4], Carlos A Camargo Jr [5]

Affiliations expand

Abstract

Study objective: To describe the demographic, clinical, and emergency medical service (EMS) response characteristics associated with EMS activations for asthma and chronic obstructive pulmonary disease (COPD) exacerbations in the US.

Methods: Using a nationwide set of out-of-hospital patient care report data from 2018 to 2019, we analyzed 9-1-1 EMS activations where asthma/COPD exacerbation was indicated by symptom, impression, or treatment provided. We excluded patients with ages less than 2 years or unknown, nonemergency transports, and encounters with any indication of anaphylaxis. Demographic, clinical, and EMS response characteristics were described for pediatric and adult patients with asthma/COPD exacerbations.

Results: A total of 1,336,988 asthma/COPD exacerbations were included, comprising 5% of qualifying 9-1-1 scene activations from 2018 to 2019. Most patients were adults (96%). Most adult patients were female (55%), whereas most pediatric patients were male (58%). Most activations occurred in urban settings (82%), particularly in pediatric patients (90%). Most asthma/COPD exacerbations were managed by advanced life support units (94%). Inhaled bronchodilators and systemic corticosteroid therapy were administered to 75% and 14% of all patients, respectively. Adults more often had oxygen saturation <92% (43% vs 20% of pediatric patients) and were more often treated with assisted ventilation (9% vs 1%).

Conclusion: In this large nationwide sample of 9-1-1 activations treated and transported by EMS, 5% were for asthma/COPD exacerbation. Future work should focus on evidence-based standardization of EMS protocols and practice for asthma/COPD exacerbations to improve the quality of EMS care.

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PLoS One

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Characterization of the external exposome and its contribution to the clinical respiratory and early biological effects in children: The PROMESA cohort study protocol

Diana Marín [1], Luz Yaneth Orozco [1][2], Diana María Narváez [3], Isabel Cristina Ortiz-Trujillo [1], Francisco José Molina [2], Carlos Daniel Ramos [2], Laura Rodriguez-Villamizar [4], Shrikant I Bangdiwala [5][6], Olga Morales [7][8], Martha Cuellar [7][9], Luis Jorge Hernández [10], Enrique Antonio Henao [11], Verónica Lopera [11], Andrea Corredor [12], María Victoria Toro [13], Helena Groot [3], Milena Villamil-Osorio [14], Diego Alejandro Muñoz [15], Roberto Carlos Hincapié [13], Ferney Amaya [13], Ana Isabel Oviedo [13], Lucelly López [1], Ricardo Morales-Betancourt [16], Beatriz Elena Marín-Ochoa [17], Oscar Eduardo Sánchez-García [13], Juan Sebastián Marín [18], José Miguel Abad [18], Julio Cesar Toro [19], Eliana Pinzón [20], Juan José Builes [21], Zulma Vanessa Rueda [1][22]

Affiliations expand

- PMID: 36662732

- DOI: 10.1371/journal.pone.0278836

Abstract

Background: Air pollution contains a mixture of different pollutants from multiple sources. However, the interaction of these pollutants with other environmental exposures, as well as their harmful effects on children under five in tropical countries, is not well known.

Objective: This study aims to characterize the external exposome (ambient and indoor exposures) and its contribution to clinical respiratory and early biological effects in children.

Materials and methods: A cohort study will be conducted on children under five (n = 500) with a one-year follow-up. Enrolled children will be followed monthly (phone call) and at months 6 and 12 (in person) post-enrolment with upper and lower Acute Respiratory Infections (ARI) examinations, asthma development, asthma control, and genotoxic

damage. The asthma diagnosis will be pediatric pulmonologist-based and a standardized protocol will be used. Exposure, effect, and susceptibility biomarkers will be measured on buccal cells samples. For environmental exposures PM2.5 will be sampled, and questionnaires, geographic information, dispersion models and Land Use Regression models for PM2.5 and NO2 will be used. Different statistical methods that include Bayesian and machine learning techniques will be used for the ambient and indoor exposures-and outcomes. This study was approved by the ethics committee at Universidad Pontificia Bolivariana.

Expected study outcomes/findings: To estimate i) The toxic effect of particulate matter transcending the approach based on pollutant concentration levels; ii) The risk of developing an upper and lower ARI, based on different exposure windows; iii) A baseline of early biological damage in children under five, and describe its progression after a one-year follow-up; and iv) How physical and chemical PM2.5 characteristics influence toxicity and children's health.

Conflict of interest statement

JCT is the owner and CEO of ATB SERVICE SAS. He does not have access to any children's information and the Environmental information is transmitted in real time and the data will be public. JMA and SM are employed by the Healthcare Company, SURA. JJB is employed by GENES laboratory. This does not alter our adherence to PLOS ONE policies on sharing data and materials. The other authors do not have conflicts of interest to declare

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Associations between interleukin 17A and 17F polymorphisms and asthma susceptibility: A meta-analysis

Young Ho Lee [1], Gwan Gyu Song [1]

Affiliations expand

- PMID: 36658661

- DOI: 10.1111/iji.12611

Abstract

Owing to their role in inflammatory reactions and immunological responses as well as their chromosomal location, interleukin (IL) 17A and 17F are regarded as candidate causal genes associated with asthma. The aim of this study was to determine whether IL17 polymorphisms are associated with susceptibility to asthma. We used the PubMed/Medline and Embase databases to search for studies reporting IL17 polymorphisms in patients with asthma and healthy controls. Meta-analyses were conducted to determine the associations between IL17A rs8193036 (-737C/T), rs2275913 (-197G/A), rs3819024 (A/G), rs3748067 (C/T), and rs4711998 (A/G) and IL17F rs763780 (7488A/G), rs2397084 (T/C), rs1889570 (C/T), rs11465553 (G/A), and rs1266828 (T/C) polymorphisms and asthma susceptibility. A total of 20 studies were included in this meta-analysis. Our results revealed the IL17A rs8193036 CC genotype was associated with asthma susceptibility (odds ratio [OR] = 1.490, 95% confidence interval [CI] = 1.027-2.161, p = .036). However, stratification by ethnicity indicated no association between this polymorphism and asthma in European and Asian subjects. Furthermore, no association was found between this polymorphism and asthma using the allele contrast, dominant or homozygous contrast models. No evidence of an association was found between any of the other IL17A and IL17F polymorphisms and asthma susceptibility in this meta-analysis. This meta-analysis showed that, among the studied polymorphisms, only the CC genotype of IL17A rs8193036 is associated with asthma susceptibility.

Keywords: asthma; interleukin 17; meta-analysis; polymorphism.

- 55 references

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Review

The molecular mechanisms of remodeling in asthma, COPD and IPF with a special emphasis on the complex role of Wnt5A

Abhinav Singla [1][2], Sebastian Reuter [1], Christian Taube [1], Marcus Peters [3], Karin Peters [2]

Affiliations expand

- PMID: 36658268

- DOI: 10.1007/s00011-023-01692-5

Abstract

Introduction: Chronic inflammatory lung diseases are a common cause of suffering and death. Chronic obstructive pulmonary disease (COPD) is the reason for 6% of all deaths worldwide. A total of 262 million people are affected by asthma and 461,000 people died in 2019. Idiopathic pulmonary fibrosis (IPF) is diagnosed in 3 million people worldwide, with an onset over the age of 50 with a mean survival of only 24-30 months. These three diseases have in common that remodeling of the lung tissue takes place, which is responsible for an irreversible decline of lung function. Pathological lung remodeling is mediated by a complex interaction of different, often misguided, repair processes

regulated by a variety of mediators. One group of these, as has recently become known, are the Wnt ligands. In addition to their well-characterized role in embryogenesis, this group of glycoproteins is also involved in immunological and structural repair processes. Depending on the combination of the Wnt ligand with its receptors and co-receptors, canonical and noncanonical signaling cascades can be induced. Wnt5A is a mediator that is described mainly in noncanonical Wnt signaling and has been shown to play an important role in different inflammatory diseases and malignancies.

Objectives: In this review, we summarize the literature available regarding the role of Wnt5A as an immune modulator and its role in the development of asthma, COPD and IPF. We will focus specifically on what is known about Wnt5A concerning its role in the remodeling processes involved in the chronification of the diseases.

Conclusion: Wnt5A has been shown to be involved in all three inflammatory lung diseases. Since the ligand affects both structural and immunological processes, it is an interesting target for the treatment of lung diseases whose pathology involves a restructuring of the lung tissue triggered in part by an inflammatory immune response.

Keywords: Airway remodeling; Asthma; Chronic obstructive pulmonary disease; Idiopathic pulmonary fibrosis; Member 5A; Wingless-Type MMTV Integration Site Family.

- 81 references

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Publication types, Grant supportexpand

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Review

Pharmacol Ther

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. 2023 Jan 16;108348.

Interleukin-4 as a therapeutic target

[Yvonne Gärtner](#) [1], [Lynn Bitar](#) [1], [Frauke Zipp](#) [1], [Christina Francisca Vogelaar](#) [2]

Affiliations expand

- PMID: 36657567

- DOI: [10.1016/j.pharmthera.2023.108348](#)

Abstract

Interleukin-4 (IL-4) is a pleiotropic cytokine mainly known for its role in type 2 immunity. Therapies antagonizing or blocking IL-4 activity have been developed to counteract diseases such as atopic dermatitis and asthma. In contrast, other disorders experimentally benefit from IL-4-related effects and IL-4 recently demonstrated beneficial activity in experimental stroke, spinal cord injury and the animal model of multiple sclerosis. To exploit IL-4-related activity for therapeutic concepts, current experimental efforts include modifying the pathway without inducing type 2 immune response and targeting of the cytokine to specific tissues. Here, we review different activities of IL-4 as well as therapeutic strategies.

Keywords: Central nervous system; Interleukin-4; Neuroprotection and -repair; Translation; Type 2 inflammation.

Conflict of interest statement

Declaration of Competing Interest The authors declare no competing interests.

SUPPLEMENTARY INFO

Publication typesexpand

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Characterization and cluster analyses of elderly asthma in comparison with non-elderly asthma patients in Japan

Maho Suzukawa [1], Ken Ohta [2], Hiroya Hashimoto [3], Yoshitaka Oyamada [4], Mari Miki [5], Mitsumasa Ogawara [6], Yoshikazu Inoue [7], Akiko M Saito [8], Yuma Fukutomi [9], Nobuyuki Kobayashi [10], Masami Taniguchi [11]; NHOM-Asthma study group [12]

Affiliations expand

- PMID: 36657562

- DOI: 10.1016/j.anai.2023.01.003

Abstract

Background: Asthma is a heterogeneous disease with multiple phenotypes that are useful in precision medicine. As the population ages, the elderly asthma (EA, aged ≥65 years) population is growing, and is now a major health problem worldwide.

Objective: The present study aimed to characterize EA and identify its phenotypes.

Methods: In adult patients with asthma (aged ≥18 years) who had been diagnosed with asthma at least 1 year prior to study enrollment, 1925 were included in the NHOM-Asthma (registered in UMIN-CTR; UMIN000027776), and the data were used for this study, JFGE-Asthma (registered in UMIN-CTR; UMIN000036912). Data from EA and non-EA (NEA) groups were compared, Ward's minimum-variance hierarchical clustering method, and principal component analysis (PCA) was performed.

Results: EA was characterized by older asthma onset, longer asthma duration and smoking history, more comorbidities, lower pulmonary function, less atopic, lower adherence, and more hospital admissions due to asthma. In contrast, the number of eosinophils, total IgE level, oral corticosteroid use, and asthma control questionnaire were equivalent between EA and NEA. There were three distinct phenotypes in EA: EA1: youngest, late-onset, short-duration, mild; EA 2: early onset, long-duration, atopic, low lung function, moderate; and EA 3: oldest, eosinophilic, over-weight, low lung function, most-severe. The classification factors of EA phenotypes included the age of onset and ACQ-6. Similarities were observed between EA and NEA phenotypes following PCA.

Conclusion: The EA in Japan may be unique because of the populations high longevity. Characterization of EA phenotypes from the present cohort indicated the need for distinct precision medicine for EA.

Keywords: asthma; cluster analysis; elderly; phenotype; tree analysis.

Conflict of interest statement

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Association between Galectin-13 Expression and Eosinophilic Airway Inflammation in Chronic Obstructive Pulmonary Disease

Lingling Yi [1][2], Yuchen Feng [1][2], Dian Chen [1][2], Yanling Jin [3], Shuchen Zhang [4]

Affiliations expand

- PMID: 36656660

- DOI: 10.1080/15412555.2022.2162377

Abstract

Chronic obstructive pulmonary disease (COPD) and asthma are chronic inflammatory diseases of the airways. Galectin-13 has recently been forwarded as a biomarker for airway eosinophilic inflammation in asthma. However, the association between galectin-13 and COPD remains unknown. To examine the changes in galectin-13 expression in acute exacerbations of COPD (AECOPD) and the stable phase of COPD and unveil the association between galectin-13 expression and eosinophilic inflammation in COPD, we measured plasma galectin-13 expression in different phases of COPD patients (n = 60, 44 AECOPD patients, and 16 stable COPD patients) and healthy controls (n = 15). Plasma levels of galectin-13 in 60 COPD patients were further analyzed and compared to systemic inflammation, airway eosinophilic inflammation, and lung function. The plasma galectin-13 level was markedly increased in subjects with AECOPD compared to stable COPD patients and healthy controls. Plasma galectin-13 levels in COPD subjects were positively correlated with serum CRP (r_s = 0.46, p = 0.0003), peripheral blood eosinophilia count (r_s = 0.57, $p < 0.0001$), and FeNO (r_s = 0.46, p = 0.0002). In addition, the level of galectin-13 was negatively correlated with FEV_1 (r_s = -0.43, p = 0.0001), FEV_1 pred (%) (r_s = -0.544, $p < 0.0001$), as well as FEV_1/FVC (r_s = -0.46, $p < 0.0001$). Multiple linear regression analysis suggested that plasma galectin-13 levels were affected by FEV_1 pred (%),

peripheral blood eosinophilia count, and FeNO. We concluded that galectin-13 levels were increased in COPD patients, and elevated galectin-13 expressions related to airway eosinophilic inflammation. Galectin-13 may facilitate the identification of COPD endotypes and may become a potential therapeutic target.

Keywords: CRP; chronic obstructive pulmonary disease; eosinophilic inflammation; galectin-13.

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Mechanistic Links Between Obesity and Airway Pathobiology Inform Therapies for Obesity-Related Asthma

Silvia Cabrera Guerrero [1], Reynold A Panettieri Jr [2], Deepa Rastogi [3]

Affiliations expand

- PMID: 36656428

Abstract

Obesity-related asthma is associated with a high disease burden and a poor response to existent asthma therapies, suggesting that it is a distinct asthma phenotype. The proposed mechanisms that contribute to obesity-related asthma include the effects of the mechanical load of obesity, adipokine perturbations, and immune dysregulation. Each of these influences airway smooth muscle function. Mechanical fat load alters airway smooth muscle stretch affecting airway wall geometry, airway smooth muscle contractility, and agonist delivery; weight loss strategies, including medically induced weight loss, counter these effects. Among the metabolic disturbances, insulin resistance and free fatty acid receptor activation influence distinct signaling pathways in the airway smooth muscle downstream of both the M2 muscarinic receptor and the β_2 adrenergic receptor, such as phospholipase C and the extracellular signal-regulated kinase signaling cascade. Medications that decrease insulin resistance and dyslipidemia are associated with a lower asthma disease burden. Leptin resistance is best understood to modulate muscarinic receptors via the neural pathways but there are no specific therapies for leptin resistance. From the immune perspective, monocytes and T helper cells are involved in systemic pro-inflammatory profiles driven by obesity, notably associated with elevated levels of interleukin-6. Clinical trials on tocilizumab, an anti-interleukin antibody, are ongoing for obesity-related asthma. This armamentarium of therapies is distinct from standard asthma medications, and once investigated for its efficacy and safety among children, will serve as a novel therapeutic intervention for pediatric obesity-related asthma. Irrespective of the directionality of the association between asthma and obesity, airway-specific mechanistic studies are needed to identify additional novel therapeutic targets for obesity-related asthma.

- 164 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

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Nighttime continuous contactless smartphone-based cough monitoring for the ward: A validation study

Filipe Barata [1], David Cleres [1], Peter Tinschert [1 2], Iris Shih [1 2], Frank Rassouli [3], Maximilian Boesch [3], Martin Brutsche [3], Elgar Fleisch [1 4]

Affiliations expand

- PMID: 36655551

- DOI: 10.2196/38439

Abstract

Background: Clinical deterioration can go unnoticed in hospital wards for hours. Mobile technologies such as wearables and smartphones enable automated, continuous, non-invasive ward monitoring and allow the detection of subtle changes in vital signs. Cough holds great potential for monitoring through mobile technologies on the ward as it is not only a symptom of prevalent respiratory diseases such as asthma, lung cancer, and COVID-19 but also a predictor of acute health deterioration. In past decades, many efforts have been made to develop an automatic cough counting tool. To date, however, there is neither a standardized, sufficiently validated method nor a scalable cough monitor that can be deployed on a consumer-centric device that reports cough counts continuously. These shortcomings limit the tracking of coughing and, consequently, hinder the monitoring of disease progression in prevalent respiratory diseases such as asthma, chronic obstructive pulmonary disease, and COVID-19 in the ward.

Objective: This exploratory study involves the validation of an automated smartphone-based monitoring system for continuous cough counting in two different modes in the ward. Unlike previous studies that focused on evaluating cough detection models on unseen data, the focus of this work is to validate a holistic smartphone-based cough detection system operating in near real-time.

Methods: Automated cough counts are measured consistently on-device and on-computer, and compared with cough and non-cough sounds counted manually over eight hours long nocturnal recordings in nine patients with pneumonia in the ward. The proposed cough detection system consists primarily of an Android app running on a smartphone that detects coughs and records sounds, and secondarily of a backend that continuously receives the cough detection information and displays the hourly cough counts. Cough detection is based on an ensemble Convolutional Neural Network developed and trained on asthmatic cough data.

Results: In this validation study, a total of 72 hours of recording from nine participants with pneumonia, four of whom were infected with SARS-CoV-2, were analyzed. All recordings were subjected to manual analysis by two blinded raters. The proposed system yielded sensitivity and specificity of 72% and 99% on-device and 82% and 99% on-computer, respectively, for detecting coughs. The mean difference between the automated and human rater cough counts were -1.0, CI 95% [-12.3, 10.2] and -0.9, CI 95% [-6.5, 4.8] coughs per hour within-subject for the on-device and on-computer mode, respectively.

Conclusions: The proposed system thus represents a smartphone cough counter that can be used for continuous hourly assessment of cough frequency in the ward.

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Mycoses

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The clinical significance of Aspergillus–positive respiratory samples

Katriina Pihlajamaa [1], Veli-Jukka Anttila [2], Hodgson Ulla [1]

Affiliations expand

- PMID: 36654511

- DOI: 10.1111/myc.13566

Abstract

Background: Aspergilli moulds are frequently detected in sputum and other respiratory samples. It is not known what the significance of these findings is, or how to differentiate contamination, temporary or persistent colonization from clinical infection when Aspergilli are found in respiratory samples.

Objectives: In this study we studied the clinical significance of Aspergillus findings from respiratory samples.

Methods: We retrospectively evaluated 299 patients who had provided Aspergillus-positive respiratory samples in 2007-2016, which provided a follow-up time of 3-13 years. Data were collected from laboratory registry and Helsinki University Hospital medical records. Underlying diseases, immunosuppression, reasons for sample collection, clinical significance of positive Aspergillus culture, antifungal medication, and patient survival were assessed.

Results: Underlying pulmonary disease had 88% of patients, most commonly asthma (44%), bronchiectasis (30%) or COPD (21%). Corticosteroids (orally or inhalation therapy) prior to positive samples used 78%; the use of corticosteroids did not explain the development of Aspergillus disease. Pulmonary disease caused by Aspergillus was identified in 88 (29%) of the reviewed patients; remaining samples did not represent clinical disease. Chronic cavitary or fibrosing pulmonary aspergillosis (CCPA or CFPA) had 44 (49%) of the diseased. The probability of Aspergillus disease increased when Aspergillus-positive samples were given repeatedly within one year (p=0.001). Mortality for all reasons was 45%. The repeated positive samples did not predict survival (p=0.084), but the diagnosis of CPA did (p<0.001).

Conclusions: The possibility of Aspergillus disease increases when Aspergilli are found repeatedly, collection of samples should be repeated due to method insensitivity. Diagnosis of CPA predicted significantly lower survival.

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Minimization of ragweed allergy immunotherapy costs through use of the sublingual immunotherapy tablet in Canadian children with allergic rhinoconjunctivitis

Anne K Ellis [1], Douglas P Mack [2][3], Rémi Gagnon [4], Eva Hammerby [5], Sheena Gosain [6]

Affiliations expand

- PMID: 36653868

- PMCID: PMC9847451

Abstract

Background: Allergy immunotherapy (AIT), in the form of subcutaneous immunotherapy (SCIT) with alum-precipitated aqueous extracts, SCIT with a modified ragweed pollen allergen tyrosine adsorbate (MRPATA; Pollinex®-R), or a sublingual immunotherapy (SLIT)-tablet are options for the treatment of ragweed pollen allergic rhinoconjunctivitis (ARC) in Canadian children. A cost minimization analysis evaluated the economic implications of the use of the ragweed SLIT-tablet vs SCIT in Canadian children with ragweed ARC.

Methods: A cost minimization analysis was conducted comparing the short ragweed SLIT-tablet, 12 Amb a 1-U, preseasonally with preseasonal ragweed SCIT, annual ragweed SCIT, or MRPATA. The analysis was conducted over a time horizon of 3 years from a public payer perspective in Ontario and Quebec. Resources and costs associated with medication and services of healthcare professionals were considered for each treatment. The resource and cost input values for the model were obtained from published literature and validated by Canadian clinical experts in active allergy practice. A discount rate of 1.5% was applied. Several scenario analyses were conducted to determine the impact of many of the key base case assumptions on the outcomes.

Results: Over the total 3-year time horizon, the ragweed SLIT-tablet had a potential cost savings of $900.14 in Ontario and $1023.14 in Quebec when compared with preseasonal ragweed SCIT, of $6613.22 in Ontario and $8750.64 in Quebec when compared with annual ragweed SCIT, and $79.62 in Ontario and $429.49 in Quebec when compared with MRPATA. The ragweed SLIT-tablet had higher drug costs compared with the other AIT options, but lower costs for healthcare professional services. The lower costs for healthcare professional services with the ragweed SLIT-tablet were driven by the need for fewer office visits than SCIT. Scenario analysis indicated that costs were most impacted by including societal costs (e.g., costs associated with patient/caregiver travel and time lost). The potential cost savings of the ragweed SLIT-tablet versus SCIT and MRPATA was maintained in most scenarios.

Conclusions: In this cost minimization analysis, the ragweed SLIT-tablet provided estimated cost savings from a public payer perspective for the treatment of ragweed ARC in Canadian children compared with SCIT or MRPATA.

Keywords: Allergic rhinoconjunctivitis; Children; Cost; Ragweed; Subcutaneous immunotherapy; Sublingual immunotherapy; Tablet.

Conflict of interest statement

- [40 references]
- [1 figure]

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Review

Sci Transl Med

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. 2023 Jan 18;15(679):eadd2563.

Allergy: Mechanistic insights into new methods of prevention and therapy

Cezmi A Akdis [1][2], Mübeccel Akdis [1], Scott D Boyd [3][4], Vanitha Sampath [3], Stephen J Galli [3][4][5], Kari C Nadeau [3]

Affiliations expand

- PMID: 36652536

- DOI: 10.1126/scitranslmed.add2563

Abstract

In the past few decades, the prevalence of allergic diseases has increased worldwide. Here, we review the etiology and pathophysiology of allergic diseases, including the role of the epithelial barrier, the immune system, climate change, and pollutants. Our current understanding of the roles of early life and infancy; diverse diet; skin, respiratory, and gut barriers; and microbiome in building immune tolerance to common environmental allergens has led to changes in prevention guidelines. Recent developments on the mechanisms involved in allergic diseases have been translated to effective treatments, particularly in the past 5 years, with additional treatments now in advanced clinical trials.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Science Translational Medicine

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☐ 14

J Asthma

Does the severity of asthma affect exercise capacity and daily physical activity?

Rocco Francesco Rinaldo [1], Gianluca Imeri [2], Michele Mondoni [1], Elena Maria Parazzini [1], Beatrice Vigo [1], Alessandra Masseroni [1], Stefano Centanni [1], Fabiano Di Marco [2]

Affiliations expand

Abstract

Objective: Exercise capacity, daily physical activity, and psychological profile are crucial aspects in the management of asthmatic patients. Whether these features are expressed in a different way in mild-moderate (MMA) and severe asthma (SA) is unknown. **Methods:** In this observational cross-sectional study, patients matching the American Thoracic Society/European Respiratory Society (ATS/ERS) definition for SA underwent incremental cardiopulmonary exercise testing (CPET), full lung function testing, and an evaluation of daily step count and physical activity. Questionnaires on quality of life, general fatigue, and presence of anxiety and depression traits (Hospital Anxiety and Depression Scale - HADS) were administered. Patients were compared with a cohort of age- and gender-matched MMA patients. **Results:** We enrolled 16 SA, 17 MMA patients, and 16 healthy subjects. Compared to MMA, SA subjects showed a median (interquartile range) reduced peak oxygen consumption during CPET (20.4 (17.2-23.3) vs. 25.6 (18.5-30.3) ml/min/kg; p = 0.019), a reduced resting lung function (FEV1% of predicted 77 (67-84 vs. 96 (84-100); p < 0.001) and a pronounced anxiety trait at HADS (9.5 (3-11.7) vs. 4.0 (2.0-7.5); p = 0.023). In addition, SA patients showed a significantly higher reduction in inspiratory capacity from rest to peak (310 (160-520) vs. 110 (-65-325) ml; p = 0.031). We found no significant differences in mean daily step count or quality of life. **Conclusions:** Compared to MMA, SA patients present a reduced exercise capacity and a more pronounced anxiety trait, but not worse daily physical activity or quality of life. These aspects should be considered in the clinical management and research development of SA.

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☐ 15

Can Patients Achieve Sufficient Peak Inspiratory Flow Rate (PIFR) With Turbuhaler® during Acute Exacerbation of Asthma?

Nur Azimah Mohd Rhazi[1], Jaya Muneswarao[2], Fatimatuzzahra' Abdul Aziz[1], Baharudin Ibrahim[3], Azlan Kamalludin[4], Shahrul Aiman Soelar[5]

Affiliations expand

- PMID: 36650693

- DOI: 10.1080/02770903.2023.2169930

Abstract

IntroductionAnti-inflammatory reliever (AIR) with or without regular maintenance delivered through Turbuhaler® has been widely recommended in the GINA strategy document. These patients are not prescribed with additional reliever inhalers, but dependent on Turbuhaler® during acute asthma episodes. The peak inspiratory flow rate (PIFR) is crucial in drug delivery from a dry powder inhaler (DPI) such as Turbuhaler®. Despite its increasing usage, there are some concerns that patients on Turbuhaler® are not able to achieve adequate PIFR during acute exacerbation of asthma.ObjectiveThis study aimed to assess the PIFR at resistance settings that matched Turbuhaler® in patients with acute exacerbation of asthma.MethodologyA six-month cross-sectional study was conducted at the Emergency Department (ED) of Hospital Sultanah Bahiyah and Hospital Kulim, Kedah, Malaysia. Adult patients diagnosed with mild to moderate acute exacerbations of asthma were recruited. The PIFRs were measured using the In-Check DIAL G16 that was set to simulate the resistance of Turbuhaler® (R3). The PIFRs were assessed before (pre) and after (post) the initial bronchodilator (BD) treatment at the ED. The minimal required PIFR was defined as flow rates ≥ 30 L/min while a PIFR of 60L/min was considered as optimalResultsA total of 151 patients (81 females and 70 males) were recruited. The mean age was 37.5 years old with a range between 18 and 79 years old. The results showed that 98% (n = 148) of patients managed to achieve the minimal PIFR required for pre-BD. The mean PIFR pre-BD was 60 ± 18.5 L/min and post-BD was 70 ± 18.5 L/min. Furthermore, more than half (54%, n = 82) of the patients recorded PIFR ≥ 60L/min during pre-BD, and about three-quarters (71%, n = 92) achieved PIFR ≥ 60L/min post-BD. The PIFR showed a moderate correlation with peak expiratory flow rate (PEFR) (r= 0.55, 95% CI: 0.43-0.65, p <0.001).ConclusionThe majority of patients with asthma in the present study were able to achieve sufficient PIFR from Turbuhaler® during mild to moderate acute exacerbations.

FULL TEXT LINKS

Meta-Analysis

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The Association between Exposure to Second-Hand Smoke and Disease in the Chinese Population: A Systematic Review and Meta-Analysis

Yu Tong Wang [1], Kui Ru Hu [1], Jian Zhao [1], Fei Ling Ai [1], Yu Lin Shi [1], Xue Wei Wang [1], Wen Yi Yang [1], Jing Xin Wang [1], Li Mei Ai [1], Xia Wan [1]

Affiliations expand

- PMID: 36650679

- DOI: 10.3967/bes2023.003

Abstract

Objective: To analyze the association between exposure to second-hand smoke (SHS) and 23 diseases, categorized into four classifications, among the Chinese population.

Methods: We searched the literature up to June 30, 2021, and eligible studies were identified according to the PECOS format: Participants and Competitors (Chinese population), Exposure (SHS), Outcomes (Disease or Death), and Study design (Case-control or Cohort).

Results: In total, 53 studies were selected. The odds ratio (*OR*) for all types of cancer was 1.79 (1.56-2.05), and for individual cancers was 1.92 (1.42-2.59) for lung cancer, 1.57 (1.40-1.76) for breast cancer, 1.52 (1.12-2.05) for bladder cancer, and 1.37 (1.08-1.73) for liver cancer. The *OR* for circulatory system diseases was 1.92 (1.29-2.85), with a value of 2.29 (1.26-4.159) for stroke. The *OR* of respiratory system diseases was 1.76 (1.13-2.74), with a value of 1.82 (1.07-3.11) for childhood asthma. The original *OR*s were also shown for other diseases. Subgroup analyses were performed for lung and breast cancer. The *OR*s varied according to time period and were significant during exposure in the household; For lung cancer, the *OR* was significant in women.

Conclusion: The effect of SHS exposure in China was similar to that in Western countries, but its definition and characterization require further clarification. Studies on the association between SHS exposure and certain diseases with high incidence rates are insufficient.

Keywords: Cancer; Chinese population; Diseases of the circulatory system; Diseases of the respiratory system; Meta-analysis; Second-hand smoke; Systematic review.

SUPPLEMENTARY INFO

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Respirology

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. 2023 Jan 17.

 doi: 10.1111/resp.14453. Online ahead of print.

Severe asthma, more than that?

Fanny Wai San Ko[1]

Affiliations expand

No abstract available

Keywords: asthma; comorbidities; inducible laryngeal obstruction; treatment.

FULL TEXT LINKS

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Review

The impact of inhalers for asthma on the global climate: a systematic review of carbon footprint and clinical outcomes in Spain

J Montoro [1], D Antolín-Amérigo [2], A Izquierdo-Domínguez [3], J J Zapata [4], G González [5], A Valero [6]

Affiliations expand

- PMID: 36648318

- DOI: 10.18176/jiaci.0887

Abstract

Background: Pressurised metered-dose inhalers (pMDIs) exert some environmental impact due to their effect on CO2 emissions. There are other therapeutic alternatives with less environmental impact that are being widely used. Nevertheless, the choice of the device and the appropriate therapy should answer the clinical needs and the characteristics of the patient.

Objective: The primary objective was to estimate the impact of pMDIs, prescribed for any indication, on annual CO2 emissions in Spain. Secondly, we aimed to evaluate the potential impact of switching pMDIs to dry-powder inhalers (DPIs) in patients with asthma.

Methods: Systematic review of the evidence published between 2010-2021 was carried out. Average annual CO2 emissions of DPIs and pMDIs were calculated in two scenarios: present and a hypothetical situation involving a switch from all pMDIs to DPIs. The impact of the switch on clinical outcomes was also evaluated.

Results: The total value of CO2-eq/year due to DPIs and pMDIs accounts for 0.0056% and 0.0909%, respectively, of total emissions in Spain. In the event of a conversion of all pMDIs to DPIs, except those for rescue medication, these percentages would be 0.0076% and 0.0579%. The evaluation of efficacy, handling, satisfaction, safety and healthcare resources utilization was not conclusive.

Conclusions: Current CO2 emissions derived from pMDIs account for a small percentage of the total CO2 footprint in Spain. Nevertheless, there is a need for research into new and more sustainable devices. Suitability and patient clinical criteria such as age or inspiratory flow should be prioritised at inhaler prescription.

Keywords: Anti-Asthmatic Agents; Asthma; Carbon Footprint; Climate change; Environment; Global warming; Inhaler devices; Metered-Dose Inhalers.

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Airway reactance predicts static lung hyperinflation in severe asthma

L Yen-Jung [1], K Hsin-Kuo [2 3], P Sheng-Wei [2 4], F Jia-Yih [2 4], S Kang-Cheng [2 5], L Yang [1], Y Sheau-Ning [6], H Yi-Han [2 7], P Diahn-Warng [2 7]

Affiliations expand

- PMID: 36645713

- DOI: 10.18176/jiaci.0888

Abstract

Background and objectives: Static lung hyperinflation (SLH) measured by body plethysmography (Pleth) in asthma is associated with poor outcomes. The severity of SLH may be associated with small airway dysfunction (SAD), which can be measured by impulse oscillometry (IOS). This study aims to determine the correlation between SLH and SAD in patients with severe asthma and the improvement of SLH and SAD in response to treatment.

Methods: We analyzed data from patients who were enrolled in the Taiwan Severe Asthma Registry, which was a prospective observational cohort. Pleth and IOS were regularly performed. The relationship between spirometric and IOS parameters was determined. Changes in the clinical outcomes in response to treatment were analyzed.

Results: In 107 patients with severe asthma, 83 (77.6%) had SLH by increased residual volume to total lung capacity (RV/TLC) ratio. Most patients were older female with worse pulmonary function and SAD compared with those without SLH. The SAD by increased airway resistance/reactance was significantly correlated with SLH. Airway reactance at 5 Hz (X5) ≤ -0.21 [kPa/(L/s)] detected SLH with the area under the receiver operating characteristic curve of 0.84 (p < 0.0001, sensitivity = 85.2%, and specificity = 83.3%). After 12 months, patients who received add-on biologics treatment had significantly reduced exacerbation, fractional exhaled nitric oxide level, blood eosinophil counts, improved forced expiratory volume in the first second, X5, and a trend of reduced RV/TLC ratio compared with those without biologics treatment.

Conclusions: In severe asthma, airway reactance X5 could be a novel parameter to assess SLH.

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Is mild asthma truly mild? The patients' real-life setting

Gabriella Guarnieri [1], Veronica Batani [2], Gianenrico Senna [2][3], Annarita Dama [3], Andrea Vianello [1], Marco Caminati [2]

Affiliations expand

- PMID: 36633404

- DOI: 10.1080/17476348.2023.2167714

Abstract

Objectives: Asthma exacerbations and, more rarely, fatal asthma attacks have been reported in mild asthma patients, suggesting poor disease control and awareness of its potential burden. Our study aimed to explore outside the hospital/specialist setting the perspective and disease treatment behavior of patients self-reporting a mild asthma diagnosis.

Methods: Computer-Assisted Personal Interviewing (CAPI) technique was used to investigate the identified study population. Questions about diagnosis, symptoms, comorbidities, treatment strategy, ongoing assessments, and quality of life were administered.

Results: Overall, 258 patients were considered for the analysis. As the most relevant results, 22% of them reported severe respiratory symptoms, 52% experienced at least one exacerbation/year, and 7% needed Emergency Room care. Sixty-six percent of the respondents assumed as needing short-acting bronchodilators only. Of note, 22% of patients were using oral steroids (OCS) intermittently and 72% of them considered their quality of life unsatisfying.

Conclusion: Outside the hospital/specialist setting, mild asthma burden is still not negligible and the treatment approach is not correct. In particular, the reported OCS use is disproportionate. Our data suggest that mild asthma, especially when self-assessed might be other than mild, suggesting that efforts to increase disease awareness, improve the disease control limiting the OCS abuse are required.

Keywords: Mild asthma; asthma control; oral steroids; patients perception; under-treatment.

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Respiratory comorbidities in severe asthma: focus on the pediatric age

Amelia Licari [1] [2], Beatrice Andrenacci [1], Maria Elisa Di Cicco [3], Maddalena Leone [4], Gian Luigi Marseglia [1] [2], Mariangela Tosca [5]

Affiliations expand

Abstract

Introduction: Asthma comorbidities are a frequent cause of adverse outcomes, such as poor asthma control, frequent asthma attacks, reduced quality of life, and higher healthcare costs. Comorbidities are well-known treatable traits whose proper management can help achieve optimal asthma control. Although multimorbidity is frequent among asthmatics, comorbidities are still a potential cause of misdiagnosis and under or over treatments, and little is known about their impact on severe pediatric asthma.

Areas covered: We provided a comprehensive, 5-year updated review focusing on the main respiratory comorbidities in severe asthma, particularly in epidemiology, pathogenesis, and current and future therapies.

Expert opinion: Respiratory comorbidities have unique characteristics in childhood. Their management must be multidisciplinary, age-specific, and integrated. Further longitudinal studies are needed to understand better the mutual interrelation and synergistic effect between asthma and its respiratory comorbidities, the identification of common, treatable risk factors leading to potential asthma prevention, the effectiveness of actual and future target-therapies, and the correlation between long-lasting respiratory comorbidities and poor lung function trajectories.

Keywords: Asthma comorbidities; breathing pattern disorders; bronchiectasis; inducible laryngeal obstructions; obstructive sleep apnea; pediatrics; rhinitis; rhinosinusitis; severe asthma; severe asthma with fungal sensitization.

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Clinical characteristics, treatment patterns and adherence in patients with asthma on multiple inhaler triple therapy: a review of findings

Mario Cazzola [1], Luigino Calzetta [2], Barbara Rinaldi [3], Vito De Novellis [3], Paola Rogliani [1], Maria Gabriella Matera [3]

Affiliations expand

- PMID: 36629483

- DOI: 10.1080/17476348.2023.2167715

Abstract

Introduction: The value of treating asthma with the triple regimen of inhaled corticosteroid (ICS), long-acting β_2-agonist (LABA), and long-acting muscarinic antagonist (LAMA) delivered using multiple inhalers (MITT), or a single inhaler (SITT) is supported by a growing body of evidence, although research is still limited regarding the use of MITT.

Areas covered: Clinical characteristics, treatment patterns, disease burden, and persistence/adherence associated with MITT use in asthma. The MEDLINE database was searched to identify references from inception until October 2022.

Expert opinion: The use of MITT is not very frequent in asthma patients, although it improves lung function and reduces the incidence of severe exacerbations. This may be due to existing concerns about using different devices on adherence and persistence to treatment, with a negative influence on outcomes, and to the fear that the patient will discontinue ICS/LABA but not LAMA. Nevertheless, although the current trend favors the SITT approach, some physicians may be induced to prescribe MITT over SITT because it

allows the titration of individual components of triple therapy to be increased or decreased. Therefore, there is an evident need for pragmatic real-life studies to document when to prefer SITT and when MITT should be used.

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Intranasal administration of nucleus-deliverable GATA3-TMD alleviates the symptoms of allergic asthma

[Su-Hyeon Lee](#)[1], [Jung-Ho Kim](#)[2], [Yekyung Seong](#)[1], [Jae-Seung Moon](#)[1], [Yuna Kim](#)[1], [Bo-Young Shin](#)[1], [Jin-Su Shin](#)[1], [Jiyoon Park](#)[1], [Choon-Sik Park](#)[3], [Sang-Kyou Lee](#)[4]

Affiliations expand

- PMID: 36502629

- DOI: [10.1016/j.bbrc.2022.11.095](#)

Free article

Abstract

Although the T helper 2 (Th2) subset is a critical player in the humoral immune response to extracellular parasites and suppression of Th1-mediated inflammation, Th2 cells have been implicated in allergic inflammatory diseases such as asthma, allergic rhinitis, and atopic dermatitis. GATA binding protein 3 (GATA3) is a primary transcription factor that mediates Th2 differentiation and secretion of Th2 cytokines, including IL-4, IL-5, and IL-13. Here, a nucleus-deliverable form of GATA3-transcription modulation domain (TMD) (ndG3-TMD) was generated using Hph-1 human protein transduction domain (PTD) to modulate the transcriptional function of endogenous GATA3 without genetic manipulation. ndG3-TMD was shown to be efficiently delivered into the cell nucleus quickly without affecting cell viability or intracellular signaling events for T cell activation. ndG3-TMD exhibited a specific inhibitory function for the endogenous GATA3-mediated transcription, such as Th2 cell differentiation and Th2-type cytokine production. Intranasal administration of ndG3-TMD significantly alleviated airway hyperresponsiveness, infiltration of immune cells, and serum IgE level in an OVA-induced mouse model of asthma. Also, Th2 cytokine secretion by the splenocytes isolated from the ndG3-TMD-treated mice substantially decreased. Our results suggest that ndG3-TMD can be a new therapeutic reagent to suppress Th2-mediated allergic diseases through intranasal delivery.

Keywords: Asthma; GATA3; Intranasal administration; Intranuclear delivery; Protein transduction domain; T helper type 2 cells.

Conflict of interest statement

Declaration of competing interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Su-Hyeon Lee reports financial support was provided by Good T Cells, Inc. Sang-Kyou Lee reports financial support was provided by Good T Cells, Inc. Jung-Ho Kim reports was provided by Good T Cells, Inc. Sang-Kyou Lee has patent pending to Sang-Kyou Lee.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Editorial

Gastroesophageal Reflux, Atopic Dermatitis, and Asthma: Finally Evidence for Causal Links?

Meghan D Althoff [1], Sunita Sharma [1]

Affiliations expand

- PMID: 36301927

- DOI: 10.1164/rccm.202210-1953ED

No abstract available

Comment on

- [Mendelian Randomization Analysis Reveals a Complex Genetic Interplay among Atopic Dermatitis, Asthma, and Gastroesophageal Reflux Disease.](#)
  Ahn K, Penn RB, Rattan S, Panettieri RA Jr, Voight BF, An SS.Am J Respir Crit Care Med. 2023 Jan 15;207(2):130-137. doi: 10.1164/rccm.202205-0951OC.PMID: 36214830

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

Association between cold weather, influenza infection, and asthma exacerbation in adults in Hong Kong

Xi Xiong [1], Yuchen Wei [2], Holly Ching Yu Lam [3], Carlos King Ho Wong [4], Steven Yuk Fai Lau [5], Shi Zhao [6], Jinjun Ran [7], Conglu Li [5], Xiaoting Jiang [5], Qianying Yue [5], Wei Cheng [8], Huwen Wang [5], Yawen Wang [5], Ka Chun Chong [9]

Affiliations expand

- PMID: 36240934

- DOI: 10.1016/j.scitotenv.2022.159362

Abstract

Despite a conspicuous exacerbation of asthma among patients hospitalized due to influenza infection, no study has attempted previously to elucidate the relationship between environmental factors, influenza activity, and asthma simultaneously in adults. In this study, we examined this relationship using population-based hospitalization records over 22 years. Daily numbers of hospitalizations due to asthma in adults of 41 public hospitals in Hong Kong during 1998-2019 were obtained. The data were matched with meteorological records and air pollutant concentrations. We used type-specific and all-

type influenza-like illness plus (ILI+) rates as proxies for seasonal influenza activity. Quasi-Poisson generalized additive models together with distributed-lag non-linear models were used to examine the association. A total of 212,075 hospitalization episodes due to asthma were reported over 22 years. The cumulative adjusted relative risk (ARR) of asthma hospitalizations reached 1.15 (95 % confidence interval [CI], 1.12-1.18) when the ILI+ total rate increased from zero to 20.01 per 1000 consultations. Compared with the median temperature, a significantly increased risk of asthma hospitalization (cumulative ARR = 1.10, 95 % CI, 1.05-1.15) was observed at the 5th percentile of temperature (i.e., 14.6 °C). Of the air pollutants, oxidant gas was significantly associated with asthma, but only at its extreme level of concentrations. In conclusion, cold conditions and influenza activities are risk factors to asthma exacerbation in adult population. Influenza-related asthma exacerbation that appeared to be more common in the warm and hot season, is likely to be attributable to influenza A/H3N2. The heavy influence of both determinants on asthma activity implies that climate change may complicate the asthma burden.

Keywords: Influenza; Pollution; Statistical model; Temperature; Weather.

Conflict of interest statement

Declaration of competing interest None of the authors have any conflict of interest to declare.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Review

Eur Respir J

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Narrative review to capture patients' perceptions and opinions about non-response and response to biological therapy for severe asthma

Courtney Coleman [1], Ekaterina Khaleva [2], Anna Rattu [2], Betty Frankemölle [3], Hanna Nielsen [4], Graham Roberts [2], Clare Williams [3]; 3TR Respiratory Work Package

Affiliations expand

- PMID: 36104293

- PMCID: PMC9849704

- DOI: 10.1183/13993003.00837-2022

Free PMC article

Abstract

Background: There are now many biological therapies to treat severe asthma. To assess which work best for which patient, we need to develop definitions of response. This narrative review aims to capture severe asthma patients' perceptions about non-response and response to biological therapy.

Methods: Four bibliographic databases were searched from inception to September 2021. Grey literature was searched with the involvement of patient representatives. A thematic approach was used for synthesis. No qualitative studies specifically explore patients' perspectives on response to biological therapy for severe asthma. Three papers and one published asthma patient interview were included. Relevant grey literature was included from online discussion forums, blogs and social media websites.

Results: Adult patients framed positive response to biological therapy in terms of reduced burden of disease and treatment. Both were multifaceted. Some patients experienced

reduced benefit from biological therapy over time. There was a group of patients who described a limited response or non-response to biological therapy. This was framed within the context of continuing hospitalisation and oral corticosteroid treatment. The speed of onset of benefit was felt to be important by some.

Conclusions: Definitions of non-response and response need to be patient-centred, yet there is a complete lack of qualitative research focused on this topic. By combining relevant published and grey literature we have provided a description of adult patients' perceptions of response to biological therapy in severe asthma. We now need to understand the views of children and adolescents with severe asthma and their carers, and diverse patient experiences in real-world settings.

Conflict of interest statement

- Cited by 1 article
- 29 references
- 2 figures

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Am J Respir Crit Care Med

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Health Care Spending on Respiratory Diseases in the United States, 1996–2016

Kevin I Duan [1] [2], Maxwell Birger [3], David H Au [1] [2], Laura J Spece [1] [2], Laura C Feemster [1] [2], Joseph L Dieleman [4]

Affiliations expand

Abstract

Rationale: Respiratory conditions account for a large proportion of health care spending in the United States. A full characterization of spending across multiple conditions and over time has not been performed. **Objectives:** To estimate health care spending in the United States for 11 respiratory conditions from 1996 to 2016, providing detailed trends and an evaluation of factors associated with spending growth. **Methods:** We extracted data from the Institute of Health Metrics and Evaluation's Disease Expenditure Project Database, producing annual estimates in spending for 38 age and sex groups, 7 types of care, and 3 payer types. We performed a decomposition analysis to estimate the change in spending associated with changes in each of five factors (population growth, population aging, disease prevalence, service usage, and service price and intensity). **Measurements and Main Results:** Total spending across all respiratory conditions in 2016 was $170.8 billion (95% confidence interval [CI], $164.2-179.2 billion), increasing by $71.7 billion (95% CI, $63.2-80.8 billion) from 1996. The respiratory conditions with the highest spending in 2016 were asthma and chronic obstructive pulmonary disease, contributing $35.5 billion (95% CI, $32.4-38.2 billion) and $34.3 billion (95% CI, $31.5-37.3 billion), respectively. Increasing service price and intensity were associated with 81.4% (95% CI, 70.3-93.0%) growth from 1996 to 2016. **Conclusions:** U.S. spending on respiratory conditions is high, particularly for chronic conditions like asthma and chronic obstructive pulmonary disease. Our findings suggest that service price and intensity, particularly for pharmaceuticals, should be a key focus of attention for policymakers seeking to reduce health care spending growth.

Keywords: health economics; health expenditures; health policy.

Comment in

- [How Much Does the United States Spend on Respiratory Diseases?](#)
  Nurmagambetov TA.Am J Respir Crit Care Med. 2023 Jan 15;207(2):126-127. doi:
  10.1164/rccm.202209-1696ED.PMID: 36155100 No abstract available.

RHINITIS

1
Review

Might biologics serve to interrupt the atopic march?

[Jonathan M Spergel](#)[1], [George Du Toit](#)[2], [Carla M Davis](#)[3]

Affiliations expand

Abstract

The atopic march was described more than 20 years ago on the basis of initial observations, and it is now seen in prospective studies. The concept has evolved and is now considered to be the progression of atopic dermatitis to other atopic conditions, including asthma, allergic rhinitis, food allergy, and eosinophilic esophagitis in a nonlinear fashion. The progression can include some or all of the aforementioned atopic conditions. The pathogenesis is part of the classic type 2 inflammatory process involving IL-4, IL-5, and IL-13 preceded by induction of the alarmins (thymic stromal lymphopoietin, IL-33, and IL-25), leading to production of IgE in a genetically predisposed individual. The development of new biologics that interact with T2 pathway represent possible ways to prevent or modify the atopic march.

Keywords: Atopic dermatitis; T2 pathway; allergic rhinitis; asthma; atopic march; biologics; eosinophilic esophagitis; food allergy.

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Allergy

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. 2023 Jan 20.

Varying effects of greenness in the spring and summer on the development

of allergic rhinitis up to 27 years of age: The Espoo Cohort Study

Inês Paciência [1][2], Aino K Rantala [1][2], Harri Antikainen [3], Timo Hugg [1][2], Maritta S Jaakkola [1][2], Jouni J K Jaakkola [1][2][4]

Affiliations expand

No abstract available

Keywords: Allergic rhinitis; early life; greenspaces; population-based cohort study; season.

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World Trade Center Health Program best practices for diagnosing and treating chronic rhinosinusitis

Rafael E de la Hoz [1], Michael R Shohet [2]

Abstract

The most frequent adverse physical health effect among World Trade Center Health Program (WTCHP) members is chronic rhinosinusitis (CRS), with some evidence supporting its association with the exposures to dust, gases, and toxicants. We selected the International Consensus Statement on Allergy and Rhinology: Rhinosinusitis (ICARS-RS-2021) as a comprehensive evidence-based guide on best practices for CRS diagnosis and treatment for the WTCHP.

Keywords: Chronic rhinitis; World Trade Center attack, 2001; chronic sinusitis; occupational medicine; smoke inhalation injury.

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Med Lett Drugs Ther

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. 2023 Jan 23;65(1668):12-14.

 doi: 10.58347/tml.2023.1668c.

Olopatadine/mometasone (Ryaltris) for allergic rhinitis

No authors listed

No abstract available

Keywords: Astepro Allergy; Dymista; Flonase Allergy Relief; Nasonex; Patanase; Ryaltris; adverse effects; allergic rhinitis; antihistamines; azelastine; azelastine/fluticasone propionate; corticosteroids; dosage; drug interactions; efficacy; fluticasone propionate; lactation; mometasone; olopatadine; pregnancy; safety.

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The Medical Letter
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Respiratory comorbidities in severe asthma: focus on the pediatric age

Amelia Licari [1][2], Beatrice Andrenacci [1], Maria Elisa Di Cicco [3], Maddalena Leone [4], Gian Luigi Marseglia [1][2], Mariangela Tosca [5]

Affiliations expand

Abstract

Introduction: Asthma comorbidities are a frequent cause of adverse outcomes, such as poor asthma control, frequent asthma attacks, reduced quality of life, and higher healthcare costs. Comorbidities are well-known treatable traits whose proper management can help achieve optimal asthma control. Although multimorbidity is frequent among asthmatics, comorbidities are still a potential cause of misdiagnosis and under or over treatments, and little is known about their impact on severe pediatric asthma.

Areas covered: We provided a comprehensive, 5-year updated review focusing on the main respiratory comorbidities in severe asthma, particularly in epidemiology, pathogenesis, and current and future therapies.

Expert opinion: Respiratory comorbidities have unique characteristics in childhood. Their management must be multidisciplinary, age-specific, and integrated. Further longitudinal studies are needed to understand better the mutual interrelation and synergistic effect between asthma and its respiratory comorbidities, the identification of common, treatable risk factors leading to potential asthma prevention, the effectiveness of actual and future target-therapies, and the correlation between long-lasting respiratory comorbidities and poor lung function trajectories.

Keywords: Asthma comorbidities; breathing pattern disorders; bronchiectasis; inducible laryngeal obstructions; obstructive sleep apnea; pediatrics; rhinitis; rhinosinusitis; severe asthma; severe asthma with fungal sensitization.

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Biochem Biophys Res Commun

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. 2023 Jan 15;640:32-39.

Intranasal administration of nucleus-deliverable GATA3-TMD alleviates the symptoms of allergic asthma

Su-Hyeon Lee [1], Jung-Ho Kim [2], Yekyung Seong [1], Jae-Seung Moon [1], Yuna Kim [1], Bo-Young Shin [1], Jin-Su Shin [1], Jiyoon Park [1], Choon-Sik Park [3], Sang-Kyou Lee [4]

Affiliations expand

Abstract

Although the T helper 2 (Th2) subset is a critical player in the humoral immune response to extracellular parasites and suppression of Th1-mediated inflammation, Th2 cells have been implicated in allergic inflammatory diseases such as asthma, allergic rhinitis, and atopic dermatitis. GATA binding protein 3 (GATA3) is a primary transcription factor that mediates Th2 differentiation and secretion of Th2 cytokines, including IL-4, IL-5, and IL-13. Here, a nucleus-deliverable form of GATA3-transcription modulation domain (TMD) (ndG3-TMD) was generated using Hph-1 human protein transduction domain (PTD) to modulate the transcriptional function of endogenous GATA3 without genetic manipulation. ndG3-TMD was shown to be efficiently delivered into the cell nucleus quickly without affecting cell viability or intracellular signaling events for T cell activation. ndG3-TMD exhibited a specific inhibitory function for the endogenous GATA3-mediated transcription, such as Th2 cell differentiation and Th2-type cytokine production. Intranasal administration of ndG3-TMD significantly alleviated airway hyperresponsiveness, infiltration of immune cells, and serum IgE level in an OVA-induced mouse model of asthma. Also, Th2 cytokine secretion by the splenocytes isolated from the ndG3-TMD-treated mice substantially decreased. Our results suggest that ndG3-TMD can be a new therapeutic reagent to suppress Th2-mediated allergic diseases through intranasal delivery.

Keywords: Asthma; GATA3; Intranasal administration; Intranuclear delivery; Protein transduction domain; T helper type 2 cells.

Conflict of interest statement

Declaration of competing interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Su-Hyeon Lee reports financial support was provided by Good T Cells, Inc. Sang-Kyou Lee reports financial support was provided by Good T Cells, Inc. Jung-Ho Kim reports was provided by Good T Cells, Inc. Sang-Kyou Lee has patent pending to Sang-Kyou Lee.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

CHRONIC COUGH

Therapeutic principles and unmet needs in the treatment of cough in pediatric patients: review and expert survey

Christian Vogelberg [1], Francisco Cuevas Schacht [2], Christopher P Watling [3], Laura Upstone [3], Georg Seifert [4]

Affiliations expand

Abstract

Background: There are evidence gaps in the management of pediatric cough, particularly for acute pediatric cough. This study had two aims: to identify therapeutic principles and unmet needs in the treatment of cough in pediatric patients (internationally), and to consider the evidence required to address these unmet needs.

Methods: A MEDLINE/PubMed database search was performed to identify articles describing therapeutic principles in the treatment of pediatric cough. An online survey of international pediatric cough experts was conducted, with questions on the definitions, diagnosis, treatment, and unmet needs in pediatric cough management.

Results: Cough guidelines have differing definitions of pediatric patients (≤12-18 years), acute pediatric cough (< 2-3 weeks), and chronic pediatric cough (> 4-8 weeks). Similarly, among 18 experts surveyed, definitions varied for pediatric patients (≤10-21 years), acute pediatric cough (< 3-5 days to < 6 weeks), and chronic pediatric cough (> 2-8 weeks). Guidelines generally do not recommend over-the-counter or prescription cough medicines in acute pediatric cough, due to lack of evidence. In the expert survey, participants had differing opinions on which medicines were most suitable for treating acute pediatric cough, and noted that effective treatments are lacking for cough-related pain and sleep disruption. Overall, guidelines and experts agreed that chronic pediatric cough requires diagnostic investigations to identify the underlying cough-causing disease and thereby to guide treatment. There are unmet needs for new effective and safe treatments for acute pediatric cough, and for randomized controlled trials of existing treatments. Safety is a particular concern in this vulnerable patient population. There is also a need for better understanding of the causes, phenotypes, and prevalence of pediatric cough, and how this relates to its diagnosis and treatment.

Conclusions: Whereas pediatric cough guidelines largely align with regard to the diagnosis and treatment of chronic cough, there is limited evidence-based guidance for the management of acute cough. There is a need for harmonization of pediatric cough management, and the development of standard guidelines suitable for all regions and patient circumstances.

Keywords: Child; Cough; Guidelines; Humans; Internationality; Pediatric; Surveys and questionnaires.

- 54 references

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Cite

Principal stratification analysis to determine health benefit of indoor air pollution reduction in a randomized environmental intervention in COPD: Results from the CLEAN AIR study

Han Woo [1], Kirsten Koehler [2], Nirupama Putcha [3], Wendy Lorizio [3], Meredith McCormack [4], Roger Peng [5], Nadia N Hansel [4]

Affiliations expand

Abstract

Background: Indoor air quality represents a modifiable exposure to Chronic Obstructive Pulmonary Disease (COPD) health. In a randomized controlled trial (CLEAN AIR study), air cleaner assignment had causal effect in improving COPD outcomes. It is unclear, however, what is the treatment effect among those for whom intervention reduced air pollution and whether it was reduction in fine particulate matter ($PM_{2.5}$) or nitrogen dioxide (NO_2) that contributed to such improvement. Because pollution is a posttreatment variable, treatment effect cannot be assessed while controlling for pollution using intention-to-treat (ITT) analysis.

Objective: Using principal stratification method, we assess indoor pollutants as the intermediate variable, and determine the causal effect of reducing indoor air pollution on COPD health.

Method: In randomized controlled trial, former smokers with COPD received either active or placebo HEPA air cleaners and were followed for 6 months. Saint George's Respiratory Questionnaire (SGRQ) was the primary outcome and secondary measures included SGRQ subscales, COPD assessment test (CAT), dyspnea (mMRC), and breathlessness, cough, and sputum scale (BCSS). Indoor $PM_{2.5}$ and NO_2 were measured. Principal stratification analysis was performed to assess the treatment effect while controlling for pollution reduction.

Results: Among those showing at least 40 % $PM_{2.5}$ reduction through air cleaners, the intervention showed improvement in respiratory symptoms for the active (vs. placebo), and the size of treatment effect shown for this subgroup was larger than that for the overall sample. In this subgroup, those with active air cleaners (vs. placebo) showed 7.7 points better SGRQ (95%CI: -14.3, -1.1), better CAT (β = -5.5; 95%CI: -9.8, -1.2), mMRC (β = -0.6; 95%CI: -1.1, -0.1), and BCSS (β = -1.8; 95%CI: -3.0, -0.5). Among those showing at least 40 % NO_2 reduction through air cleaners, there was no intervention difference in outcomes.

Conclusion: Air cleaners caused clinically significant improvement in respiratory health for individuals with COPD through reduction in indoor $PM_{2.5}$.

Trial registration: ClinicalTrials.gov: NCT02236858.

Keywords: Air cleaners; COPD; Environment; Particulate matter; Principal stratification; Randomized controlled trial.

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COPD

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Cough Assessment and Management in Pulmonary Rehabilitation– A Canadian Survey

Ana Maria Ilicic [1], Dina Brooks [1][2][3], Michelle Kho [1][4][5], Roger Goldstein [2][3], Ana Oliveira [1][2][6][7]

Affiliations expand

- PMID: 36656707

- DOI: 10.1080/15412555.2022.2141622

Abstract

Pulmonary rehabilitation is a cornerstone intervention for controlling respiratory symptoms in people with chronic respiratory diseases. Chronic cough affects up to 90% of people with chronic respiratory diseases, however, it is currently unknown whether chronic cough is assessed and/or managed in pulmonary rehabilitation. This study aimed to determine if and how chronic cough is assessed and managed in pulmonary rehabilitation. This was a cross-sectional study. Pulmonary rehabilitation programs in Canada were identified *via* online websites. A representative from each program was invited to complete an online survey including the following topics: program demographics, assessment and management practices, and barriers and facilitators. Of 133 programs contacted, 31 returned a completed survey (23% response rate). Approximately half (52%) of respondents reported enrolling patients with chronic cough. Of those, 45% reported assessing and 62% reported intervening in chronic cough. Inadequate knowledge of assessment and management techniques was commonly identified to be a barrier and increased education was suggested as a possible facilitator. Based on pulmonary rehabilitation programs that responded to our survey, chronic cough is a prevalent symptom; however, it is scarcely assessed and managed. A need for structured education and the use of standardised strategies were reported as facilitators to the assessment and management of chronic cough in pulmonary rehabilitation.

Keywords: Chronic obstructive pulmonary disease (COPD); lung disease; management; questionnaire; rehabilitation.

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Nighttime continuous contactless smartphone-based cough monitoring for the ward: A validation study

Filipe Barata[1], David Cleres[1], Peter Tinschert[1][2], Iris Shih[1][2], Frank Rassouli[3], Maximilian Boesch[3], Martin Brutsche[3], Elgar Fleisch[1][4]

Affiliations expand

- PMID: 36655551

- DOI: 10.2196/38439

Abstract

Background: Clinical deterioration can go unnoticed in hospital wards for hours. Mobile technologies such as wearables and smartphones enable automated, continuous, non-invasive ward monitoring and allow the detection of subtle changes in vital signs. Cough holds great potential for monitoring through mobile technologies on the ward as it is not only a symptom of prevalent respiratory diseases such as asthma, lung cancer, and COVID-19 but also a predictor of acute health deterioration. In past decades, many efforts have

been made to develop an automatic cough counting tool. To date, however, there is neither a standardized, sufficiently validated method nor a scalable cough monitor that can be deployed on a consumer-centric device that reports cough counts continuously. These shortcomings limit the tracking of coughing and, consequently, hinder the monitoring of disease progression in prevalent respiratory diseases such as asthma, chronic obstructive pulmonary disease, and COVID-19 in the ward.

Objective: This exploratory study involves the validation of an automated smartphone-based monitoring system for continuous cough counting in two different modes in the ward. Unlike previous studies that focused on evaluating cough detection models on unseen data, the focus of this work is to validate a holistic smartphone-based cough detection system operating in near real-time.

Methods: Automated cough counts are measured consistently on-device and on-computer, and compared with cough and non-cough sounds counted manually over eight hours long nocturnal recordings in nine patients with pneumonia in the ward. The proposed cough detection system consists primarily of an Android app running on a smartphone that detects coughs and records sounds, and secondarily of a backend that continuously receives the cough detection information and displays the hourly cough counts. Cough detection is based on an ensemble Convolutional Neural Network developed and trained on asthmatic cough data.

Results: In this validation study, a total of 72 hours of recording from nine participants with pneumonia, four of whom were infected with SARS-CoV-2, were analyzed. All recordings were subjected to manual analysis by two blinded raters. The proposed system yielded sensitivity and specificity of 72% and 99% on-device and 82% and 99% on-computer, respectively, for detecting coughs. The mean difference between the automated and human rater cough counts were -1.0, CI 95% [-12.3, 10.2] and -0.9, CI 95% [-6.5, 4.8] coughs per hour within-subject for the on-device and on-computer mode, respectively.

Conclusions: The proposed system thus represents a smartphone cough counter that can be used for continuous hourly assessment of cough frequency in the ward.

[Expert consensus on the diagnosis and treatment of SARS-CoV-2-associated cough]

[Article in Chinese]

Chinese Thoracic Society; National Center for Respiratory Medicine

Abstract

in English, Chinese

Cough is a common symptom in the acute phase of novel coronavirus SARS-CoV-2 infection, and some patients may develop persistent cough (subacute cough or even chronic cough), which affects the quality of life. Currently, the Omicron variant of SARS-CoV-2 infection is still widespread in China. In order to guide physicians on the diagnosis and treatment of SARS-CoV-2-associated cough, the Asthma Group of the Chinese Thoracic Society and the National Centre for Respiratory Medicine organized relevant experts to develop the Expert Consensus on the Diagnosis and Treatment of SARS-CoV-2-associated Cough. This consensus includes five parts: epidemiology and pathogenesis, clinical manifestations, diagnosis and differential diagnosis, treatment and outlook.The incidence of acute cough is 44%-72.5%, and about one third is productive cough. Current data shows that the average duration of cough is proximately 2 weeks, but in some patients, cough could last longer, even up to several months. SARS-CoV-2 infection cough is associated with airway epithelial damage, immunogenic or neurogenic inflammation, airway mucus hypersecretion, and cough hypersensitivity (peripheral or central).The diagnosis of SARS-CoV-2-associated cough in acute phase relies on epidemiological history, clinical characteristics, physical examination, and SARS-CoV-2 antigen or nucleic acid tests. It is also important to distinguish it from cough following other respiratory

infections. The patients in acute and subacute phases of cough are currently treated symptomatically, by using cough suppressants and expectorants according to the types of the cough. For patients with severe cough, central or peripheral cough suppressants can be used. Combined first-generation antihistamines/decongestants (A/D preparations) are recommended. Anti-viral treatment such as Paxlovid is used in severe patients or patients who are likely to develop severe conditions. Anti-bacterial treatment is not recommended except for patients with bacterial infectious traits. Inhaled corticosteroids or corticosteroids plus long acting beta agonists or leukotriene antagonists are only used for patients with wheezing, or those who have asthma or allergy history, or who have evidence of eosinophilic inflammation or who are refractory to antitussive treatment. Patients who have chronic respiratory diseases such as COPD or asthma should maintain the regular treatments. With regard to TCM treatment, effectiveness is indicated both in the acute phase or non-acute phase based on clinical practice, and collection of more evidence on this aspect is also under way.There is limited data on SARS-CoV-2-associated cough in regard of epidemiology, pathogenesis, features of cough, treatment, and prognosis. More studies are warranted to improve our understanding and management of SARS-CoV-2-associated cough in the future.

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Novel α7 nicotinic acetylcholine receptor modulators as potential antitussive agents

Anatoly Mazurov [1], Jenny Ho [1], Tiffany Low [1], Julia Hoeng [2]

Affiliations expand

Abstract

A novel series of α7 nicotinic acetylcholine receptor (nAChR) modulators was designed and evaluated for antitussive activity in an in vivo guinea pig model of chemically induced cough. Compound 16 at all tested doses (9.5, 3 and 1 mg/kg) significantly ($p < 0.01$) reduced the cumulative number of coughs and showed similar results to a positive control (codeine at 30 mg/kg). Among three different administration routes (intraperitoneal, oral and inhalation), compound 16 exerted a significant antitussive effect in guinea pigs at an inhaled dose as low as 0.4 mg/kg ($p < 0.05$). α7 nAChR modulators may provide a novel, non-narcotic approach to therapy in patients with acute and chronic cough.

Keywords: Antitussive effect; In vivo guinea pig model; α7 nicotinic acetylcholine receptor modulator.

Conflict of interest statement

Declaration of Competing Interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: All authors except J.H. are employees of Philip Morris International. J.H. was an employee of Philip Morris International at the time the experiments were performed.

FULL TEXT LINKS

ELSEVIER
FULL-TEXT ARTICLE

BRONCHIECTASIS

The impact of depression and anxiety on the risk of exacerbation in adults with bronchiectasis: A prospective cohort study

Yong-Hua Gao [1][2][3], Hui-Zhen Zheng [1][2][3], Hai-Wen Lu [1][2][3], Yuan-Yuan Li [4][3], Yun Feng [5][6][3], Bei Mao [1][2], Jiu-Wu Bai [1][2], Shuo Liang [1][2], Ke-Bin Cheng [1][2], Shu-Yi Gu [1][2], Xiao-Li Sun [1][2], Jian-Xiong Li [1][2], Ai Ge [1][2], Man-Hui Li [1][2], Jia-Wei Yang [1][2], Lu Bai [4], Han-Yu Yu [4], Jie-Ming Qu [7][6], Jin-Fu Xu [8][2]

Affiliations expand

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PLoS One

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Long-term respiratory follow-up of ICU hospitalized COVID-19 patients: Prospective cohort study

Carlos Roberto Ribeiro Carvalho[1], Celina Almeida Lamas[1], Rodrigo Caruso Chate[2], João Marcos Salge[1], Marcio Valente Yamada Sawamura[2], André L P de Albuquerque[1], Carlos Toufen Junior[1], Daniel Mario Lima[3], Michelle Louvaes Garcia[1], Paula Gobi Scudeller[1], Cesar Higa Nomura[2], Marco Antonio Gutierrez[3], Bruno Guedes Baldi[1]; HCFMUSP Covid-19 Study Group

Affiliations expand

- PMID: 36662879

- DOI: 10.1371/journal.pone.0280567

Abstract

Background: Coronavirus disease (COVID-19) survivors exhibit multisystemic alterations after hospitalization. Little is known about long-term imaging and pulmonary function of hospitalized patients intensive care unit (ICU) who survive COVID-19. We aimed to investigate long-term consequences of COVID-19 on the respiratory system of patients discharged from hospital ICU and identify risk factors associated with chest computed tomography (CT) lesion severity.

Methods: A prospective cohort study of COVID-19 patients admitted to a tertiary hospital ICU in Brazil (March-August/2020), and followed-up six-twelve months after hospital admission. Initial assessment included: modified Medical Research Council dyspnea scale, SpO2 evaluation, forced vital capacity, and chest X-Ray. Patients with alterations in at least one of these examinations were eligible for CT and pulmonary function tests (PFTs) approximately 16 months after hospital admission. Primary outcome: CT lesion severity (fibrotic-like or non-fibrotic-like). Baseline clinical variables were used to build a machine learning model (ML) to predict the severity of CT lesion.

Results: In total, 326 patients (72%) were eligible for CT and PFTs. COVID-19 CT lesions were identified in 81.8% of patients, and half of them showed mild restrictive lung impairment and impaired lung diffusion capacity. Patients with COVID-19 CT findings were stratified into two categories of lesion severity: non-fibrotic-like (50.8%-ground-glass opacities/reticulations) and fibrotic-like (49.2%-traction bronchiectasis/architectural distortion). No association between CT feature severity and altered lung diffusion or functional restrictive/obstructive patterns was found. The ML detected that male sex, ICU and invasive mechanic ventilation (IMV) period, tracheostomy and vasoactive drug need during hospitalization were predictors of CT lesion

severity(sensitivity,0.78±0.02;specificity,0.79±0.01;F1-score,0.78±0.02;positive predictive rate,0.78±0.02; accuracy,0.78±0.02; and area under the curve,0.83±0.01).

Conclusion: ICU hospitalization due to COVID-19 led to respiratory system alterations six-twelve months after hospital admission. Male sex and critical disease acute phase, characterized by a longer ICU and IMV period, and need for tracheostomy and vasoactive drugs, were risk factors for severe CT lesions six-twelve months after hospital admission.

Conflict of interest statement

The authors have declared that no competing interests exist.

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Review

The clinical spectrum of aspergillosis in chronic obstructive pulmonary disease

Akaninyene Otu[1], Chris Kosmidis[2], Alexander G Mathioudakis[3][4], Chibuike Ibe[5], David W Denning[6]

Affiliations expand

- PMID: 36662439

- DOI: 10.1007/s15010-022-01960-2

Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. In this review, we present the clinical spectrum and pathogenesis of syndromes caused by Aspergillus in COPD namely invasive aspergillosis (IA), community-acquired Aspergillus pneumonia, chronic pulmonary Aspergillosis and Aspergillus sensitisation. Some of these entities are clearly linked to COPD, while others may coexist, but are less clearly liked directly to COPD. We discuss current uncertainties as these pertain to IA in COPD cohorts and explore areas for future research in this field.

- 157 references

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Comparison of Bronchial Artery Embolisation Versus Conservative Treatment for Bronchiectasis–Related Nonmassive Haemoptysis: A Single–Centre Retrospective Study

Hai-Tao Yan #1, Guang-Dong Lu #1, Jin-Xing Zhang 1, Chun-Gao Zhou 1, Jin Liu 2, Sheng Liu 1, Hai-Bin Shi 1, Qing-Quan Zu 3

Affiliations expand

- PMID: 36658375

- DOI: 10.1007/s00270-023-03361-w

Abstract

Objective: To compare the safety and effectiveness between bronchial artery embolisation (BAE) and conservative treatment for bronchiectasis-related nonmassive haemoptysis patients.

Materials and methods: From January 2015 to December 2020, consecutive bronchiectasis-related nonmassive haemoptysis patients who underwent either BAE (n = 98) or conservative treatment (n = 118) were included. Treatment-related complications, length of hospital stays, clinical success rate, patient satisfaction, and recurrence-free survival rates were compared between groups. Prognostic factors related to recurrence were also analysed.

Results: During a median follow-up time of 44.8 months (range, 2.4-83.6 months), 34 and 66 patients in the BAE and conservative treatment groups suffered relapse. The 1-year, 2-year, 3-year and 5-year haemoptysis-free survival rates in the BAE and conservative treatment groups were 79.2%, 68.1%, 62.8%, and 57.6% and 64.0%, 52.8%, 44.1%, and 37.0%, respectively (P = 0.007). The minor complication rate after BAE was higher than that after conservative treatment (23/98 vs. 12/118, P = 0.008). BAE was associated with shorter hospital stays (5.0 vs. 7.0 days, P = 0.042) and higher patient satisfaction (88.8% vs. 74.6%, P = 0.008) than those for conservative treatment and with comparable clinical success rates (95.9% vs. 91.5%, P = 0.192). Treatment type, haemoptysis duration, and bronchiectasis severity were independently significant predictors of recurrence for these patients.

Conclusions: BAE could be another option for bronchiectasis-related nonmassive haemoptysis patients. In the patients with longer duration and more severe bronchiectasis, BAE still appeared to have better long-term haemoptysis control than conservative therapy.

Keywords: Bronchiectasis; Conservative treatment; Embolisation; Haemoptysis; Recurrence; Therapeutic.

- 32 references

SUPPLEMENTARY INFO

Proceed to details

The clinical significance of Aspergillus–positive respiratory samples

[Katriina Pihlajamaa](#)[1], [Veli-Jukka Anttila](#)[2], [Hodgson Ulla](#)[1]

Affiliations expand

- PMID: 36654511

- DOI: [10.1111/myc.13566](#)

Abstract

Background: Aspergilli moulds are frequently detected in sputum and other respiratory samples. It is not known what the significance of these findings is, or how to differentiate contamination, temporary or persistent colonization from clinical infection when Aspergilli are found in respiratory samples.

Objectives: In this study we studied the clinical significance of Aspergillus findings from respiratory samples.

Methods: We retrospectively evaluated 299 patients who had provided Aspergillus-positive respiratory samples in 2007-2016, which provided a follow-up time of 3-13 years. Data were collected from laboratory registry and Helsinki University Hospital medical records. Underlying diseases, immunosuppression, reasons for sample collection, clinical significance of positive Aspergillus culture, antifungal medication, and patient survival were assessed.

Results: Underlying pulmonary disease had 88% of patients, most commonly asthma (44%), bronchiectasis (30%) or COPD (21%). Corticosteroids (orally or inhalation therapy) prior to positive samples used 78%; the use of corticosteroids did not explain the development of Aspergillus disease. Pulmonary disease caused by Aspergillus was identified in 88 (29%) of the

reviewed patients; remaining samples did not represent clinical disease. Chronic cavitary or fibrosing pulmonary aspergillosis (CCPA or CFPA) had 44 (49%) of the diseased. The probability of Aspergillus disease increased when Aspergillus-positive samples were given repeatedly within one year (p=0.001). Mortality for all reasons was 45%. The repeated positive samples did not predict survival (p=0.084), but the diagnosis of CPA did (p<0.001).

Conclusions: The possibility of Aspergillus disease increases when Aspergilli are found repeatedly, collection of samples should be repeated due to method insensitivity. Diagnosis of CPA predicted significantly lower survival.

Keywords: Allergic bronchopulmonary aspergillosis; Asthma; Bronchiectasis; COPD; Chronic infection; Invasive pulmonary aspergillosis; Lung transplantation; Pulmonary aspergillosis.

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Clinical features and markers to identify pulmonary lesions caused by infection or vasculitis in AAV patients

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Abstract

Objectives: Pulmonary lesion is frequently seen in ANCA-associated vasculitis (AAV) patients primarily due to AAV lung involvement or infection, which are hard to differentiate due to their high similarity in clinical manifestations. We aimed to analyze the clinical features of pulmonary lesions consequent to AAV involvement or infection in AAV patients and further identify the markers for differential diagnosis.

Methods: 140 AAV patients who admitted to the Renmin Hospital of Wuhan University from January 2016 to July 2021 were included in this study. According to the nature of lung conditions, these patients were divided into the non-pulmonary lesion group, the lung infection group and the non-pulmonary infection group, and their demographics, clinical symptoms, imaging features, as well as laboratory findings were compared. A receiver operating characteristic (ROC) curve was drawn, and the diagnostic efficacy of single biomarker and composite biomarkers on pulmonary infection was then evaluated.

Results: The patients in the lung infection group were significantly older than those in the no lesion group (63.19 ± 14.55 vs 54.82 ± 15.08, $p = 0.022$). Patients in the lung infection group presented more frequent symptoms and more obvious pulmonary image findings. Compared with patients in the non-pulmonary infection group, patients in the lung infection group showed a higher symptom incidence of fever, chest tightness, cough and expectoration, and hemoptysis (52.94% vs 16.00%, 61.76% vs 40.00%, 72.06% vs 46.00%, 27.94% vs 8.00%, $p < 0.05$, respectively), and more changes in pulmonary CT scanning images in terms of patched/striped compact opacity, alveolar hemorrhage, bronchiectasis, pleural effusion, as well as mediastinal lymphadenopathy (89.71% vs 52.00%, 11.76% vs 2.00%, 22.06% vs 8.00%, 50.00% vs 20.00%, 48.53% vs 24.00%, $p < 0.05$, respectively). In addition, patients in the lung infection group had significantly higher levels of serum pro-calcitonin (PCT), C-reactive protein (CRP), amyloid A (SAA), blood neutrophil-to-lymphocyte ratio (NLCR), erythrocyte sedimentation rate (ESR), as well as Birmingham vasculitis activity score (BVAS) than patients in the other two groups ($p < 0.05$). Among all biomarkers, PCT exhibited the highest diagnostic efficacy (0.928; 95%CI 0.89-0.97) for pulmonary infected AAV patients at a cut-off score of 0.235 ng/ml with 85.3% sensitivity and 84% specificity. Moreover, the composite biomarker of PCT-CRP-NLCR showed more diagnostic efficacy (0.979; 95% CI 0.95-1.00) in distinguishing the infectious and non-infectious lung injuries in AAV patients.

Conclusions: AAV patients with lung infection manifested more clinical symptoms and prominent lung image changes. The PCT and composite biomarker PCT-CRP-NLCR showed high diagnostic efficacy for a lung infection in AAV patients. Pulmonary lesion caused by either infection or AAV involvement is commonly seen and difficult to distinguish. We aim to identify the biomarkers that can be applied in the differentiation diagnosis of pulmonary lesions in AAV patients.

Keywords: ANCA-associated vasculitis (AAV); Differential diagnosis; Infection; Lung lesion.

Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Respiratory comorbidities in severe asthma: focus on the pediatric age

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Abstract

Introduction: Asthma comorbidities are a frequent cause of adverse outcomes, such as poor asthma control, frequent asthma attacks, reduced quality of life, and higher healthcare costs. Comorbidities are well-known treatable traits whose proper management can help achieve optimal asthma control. Although multimorbidity is frequent among asthmatics, comorbidities are still a potential cause of misdiagnosis and under or over treatments, and little is known about their impact on severe pediatric asthma.

Areas covered: We provided a comprehensive, 5-year updated review focusing on the main respiratory comorbidities in severe asthma, particularly in epidemiology, pathogenesis, and current and future therapies.

Expert opinion: Respiratory comorbidities have unique characteristics in childhood. Their management must be multidisciplinary, age-specific, and integrated. Further longitudinal studies are needed to understand better the mutual interrelation and synergistic effect between asthma and its respiratory comorbidities, the identification of common, treatable risk factors leading to potential asthma prevention, the effectiveness of actual and future target-therapies, and the correlation between long-lasting respiratory comorbidities and poor lung function trajectories.

Keywords: Asthma comorbidities; breathing pattern disorders; bronchiectasis; inducible laryngeal obstructions; obstructive sleep apnea; pediatrics; rhinitis; rhinosinusitis; severe asthma; severe asthma with fungal sensitization.

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