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J Integr Complement Med
.
. 2023 Feb 17.
doi: 10.1089/jicm.2022.0552. Online ahead of print.

Mind-Body Intervention for Dysfunctional Breathing in Chronic Obstructive Pulmonary Disease: Feasibility Study and Lessons Learned

Anna Migliore Norweg[1], Yinxiang Wu[2], Andrea Troxel[2], Jonathan H Whiteson[3], Eileen Collins[4], Francois Haas[3], Anne Skamai[5], Roberta Goldring[6], Girardin Jean-Louis[2,7], Joan Reibman[6], Linda Ehrlich-Jones[8], Naomi Simon[7]
Affiliations expand

- PMID: 36800224

- DOI: 10.1089/jicm.2022.0552

Abstract

Purpose: Dysfunctional breathing behaviors are prevalent in chronic obstructive pulmonary disease (COPD). Although these behaviors contribute to dyspnea, abnormal carbon dioxide (CO_2) levels, and COPD exacerbations, they are modifiable. Current dyspnea treatments for COPD are suboptimal, because they do not adequately address dysfunctional breathing behaviors and anxiety together. We developed a complementary mind-body breathlessness therapy, called capnography-assisted respiratory therapy (CART), that uses real-time CO_2 biofeedback at the end of exhalation (end-tidal CO_2 or $ETCO_2$), to target dysfunctional breathing habits and improve dyspnea treatment and pulmonary rehabilitation (PR) adherence in COPD. The study aim was to test the feasibility of integrating CART with a traditional, clinic-based PR program in an urban setting. ***Methods:*** We used a feasibility pre- and post-test design, with 2:1 randomization to CART+PR or control (PR-alone) groups, to test and refine CART. Multi-component CART consisted of six, 1-h weekly sessions of slow breathing and mindfulness exercises, $ETCO_2$ biofeedback, motivational counseling, and a home program. All participants were offered twice weekly, 1-h sessions of PR over 10 weeks (up to 20 sessions). ***Results:*** Thirty-one participants with COPD were enrolled in the study. Approximately a third of participants had symptoms of psychological distress. Results showed that CART was feasible and acceptable based on 74% session completion and 91.7% homework exercise completion (n = 22). Within-group effect sizes for CART+PR were moderate to large (Cohen's d = 0.51-1.22) for reduction in resting Borg dyspnea (anticipatory anxiety) and respiratory rate, St. George's Respiratory Questionnaire (SGRQ) respiratory symptoms; and increase in Patient-Reported Outcomes Measurement Information System (PROMIS) physical function and physical activity; all $p < 0.05$. ***Conclusions:*** CART is a new mind-body breathing therapy that targets eucapnic breathing, interoceptive function, and self-regulated breathing to relieve dyspnea and anxiety symptoms in COPD. Study findings supported the feasibility of CART and showed preliminary signals that CART may improve exercise tolerance, reduce dyspnea, and enhance PR completion by targeting reduced dysfunctional breathing patterns (CTR No. NCT03457103).

Keywords: breathing therapy; capnography biofeedback; dyspnea anxiety; interoception; pulmonary rehabilitation.

. 2023 Feb 17;1-25.
doi: 10.1080/13696998.2023.2182092. Online ahead of print.

Incidence and medical costs of chronic obstructive respiratory disease in Spanish hospitals: a retrospective database analysis

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Affiliations expand

- PMID: 36800217

- DOI: 10.1080/13696998.2023.2182092

Abstract

Objective: This study aimed to assess the comorbidity profile, use of health care resources and medical costs of patients with chronic obstructive pulmonary disease (COPD) treated at the hospital level in Spain.

Methods: Admission records of patients with COPD and at least two admissions registered between January 2016 and December 2020 were obtained from a Spanish hospital discharge database and analyzed in a retrospective multicenter study.

Results: 95,140 patients met inclusion criteria; 69.1% were males with a median age of 75 years. Mean Charlson comorbidity index (CCI) was 1.9 in the index admission, increasing to 2.1 during the follow-up period. An acute exacerbation of COPD was registered in 93.6% of patients in the index admission; other secondary diagnoses included respiratory failure (56.8%), essential hypertension (36.9%), hypercholesterolemia (26.7%) and diabetes (26.3%). The age-adjusted incidence rate of COPD was 22.6 per 10,000 persons over the study period, decreasing significantly the year 2020. Mortality rate was 4.1% for COPD patients, increasing to 6.6% the year 2020. The year 2020, 191 patients registered a COVID-19 infection, with a mortality rate of 23.0%. Length of hospital stay, and intensive care unit (ICU) stay increased in the follow-up period versus the index admission, similarly to admission costs. Mean admission cost was €3212 in the index admission, with cost increases being associated with age, length of stay, ICU stay and CCI.

Conclusions: Patients' condition worsened significantly over the follow-up period, in terms of comorbidity and dependence on respirator, with an increased mortality rate and higher admission costs.

Keywords: COPD; I; I1; I10; I11; Spain; chronic obstructive pulmonary disease; comorbidity; incidence; mortality.

Review

Adv Biol (Weinh)

. 2023 Feb 16;e2200292.
doi: 10.1002/adbi.202200292. Online ahead of print.

Circadian Disruption in Night Shift Work and Its Association with Chronic Pulmonary Diseases

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Affiliations expand

- PMID: 36797209

- DOI: 10.1002/adbi.202200292

Abstract

Globalization and the expansion of essential services over continuous 24 h cycles have necessitated the adaptation of the human workforce to shift-based schedules. Night shift work (NSW) causes a state of desynchrony between the internal circadian machinery and external environmental cues, which can impact inflammatory and metabolic pathways. The discovery of clock genes in the lung has shed light on potential mechanisms of circadian misalignment in chronic pulmonary disease. Here, the current knowledge of circadian clock disruption caused by NSW and its impact on lung inflammation and associated pathophysiology in chronic lung diseases, such as asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, and COVID-19, is reviewed. Furthermore, the limitations of the current understanding of circadian disruption and potential future chronotherapeutic advances are discussed.

Keywords: asthma; chronic obstructive pulmonary disease; circadian disruption; clock genes; night shift work; pulmonary fibrosis.

- 119 references

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Brain Behav Immun

. 2023 Feb 14;S0889-1591(23)00034-X.
doi: 10.1016/j.bbi.2023.02.009. Online ahead of print.

Lung function and risk of incident dementia: a prospective cohort study of 431,834 individuals

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Affiliations expand

- PMID: 36796705

- DOI: 10.1016/j.bbi.2023.02.009

Abstract

Background: Whether lung function prospectively affects cognitive brain health independent of their overlapping factors remains largely unknown. This study aimed to investigate the longitudinal association between decreased lung function and cognitive brain health and to explore underlying biological and brain structural mechanisms.

Methods: This population-based cohort included 43,1834 non-demented participants with spirometry from the UK Biobank. Cox proportional hazard models were fitted to estimate the risk of incident dementia for individuals with low lung function. Mediation models were regressed to explore the underlying mechanisms driven by inflammatory markers, oxygen-carrying indices, metabolites, and brain structures.

Findings: During a follow-up of 3,736,181 person-years (mean follow-up 8.65 years), 5,622 participants (1.30%) developed all-cause dementia, which consisted of 2,511 Alzheimer's dementia (AD) and 1,308 Vascular Dementia (VD) cases. Per unit decrease in lung function measure was each associated with increased risk for all-cause dementia (forced expiratory volume in 1 second [liter]: hazard ratio [HR, 95%CI], 1.24 [1.14-1.34], $P=1.10\times10^{-07}$; forced vital capacity [liter]: 1.16 [1.08-1.24], $P=2.04\times10^{-05}$; peak expiratory flow [liter/min]: 1.0013 [1.0010-1.0017], $P=2.73\times10^{-13}$). Low lung function generated similar hazard estimates for AD and VD risks. As underlying biological mechanisms, systematic inflammatory markers, oxygen-carrying indices, and specific metabolites mediated the effects of lung function on dementia risks. Besides, brain grey and white matter patterns mostly affected in dementia were substantially changed with lung function.

Interpretation: Life-course risk for incident dementia was modulated by individual lung function. Maintaining optimal lung function is useful for healthy aging and dementia prevention.

Keywords: Brain structure; Chronic obstructive pulmonary disease; Dementia; Lung function.

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.

Rev Clin Esp (Barc)

. 2023 Feb 14;S2254-8874(23)00025-5.

doi: 10.1016/j.rceng.2023.02.003. Online ahead of print.

Disfunción eréctil en pacientes con EPOC. Una revisión sistemática y metaanálisis

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Affiliations expand

- PMID: 36796633

- DOI: 10.1016/j.rceng.2023.02.003

Abstract

Introduction: Studies on sexuality in patients with chronic obstructive pulmonary disease (COPD) are scarce and have yielded conflicting results. Our aim was to determine the prevalence of erectile dysfunction (ED) and associated factors in patients with COPD.

Methods: Articles with data on ED prevalence in patients diagnosed with COPD through spirometry were searched for in the PubMed, Embase, Cochrane Library, and Virtual Health Library databases from the year of their creation until January 31, 2021. The prevalence of ED was assessed with a weighted mean of the studies. A meta-analysis was performed using the Peto fixed-effect model to evaluate the association of COPD with ED.

Results: Fifteen studies were ultimately included. The weighted prevalence of ED was 74.6%. A meta-analysis with four studies and 519 individuals showed an association of COPD with ED (estimated weighted odds ratio 2.89, 95% CI 1.93-4.32, $p < 0.001$), with a non-negligible degree of heterogeneity (I^2 57%). In the systematic review, age, smoking, degree of obstruction, oxygen saturation, and previous health status were associated with a higher prevalence of ED.

Conclusions: ED is common in patients with COPD and its prevalence is higher than in the general population.

Keywords: COPD; Disfunción eréctil; Disfunción sexual; EPOC; Erectile dysfunction; Sexual dysfunction.

J Pain Symptom Manage

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. 2023 Feb 13;S0885-3924(23)00041-6.

doi: 10.1016/j.jpainsymman.2023.01.014. Online ahead of print.

Specialist palliative care referral practices among oncologists, cardiologists, respirologists: a comparison of national survey studies

Michael Bonares[1], Lisa W Le[2], Camilla Zimmermann[3], Kristen Wentlandt[4]
Affiliations expand

- PMID: 36796528

- DOI: 10.1016/j.jpainsymman.2023.01.014

Abstract

Context: Although patients with non-malignant diseases have palliative care needs similar to those of cancer patients, they are less likely to receive specialist palliative care. Referral practices of oncologists, cardiologists, and respirologists could provide insight into reasons for this difference.

Objectives: We compared referral practices to specialist palliative care among cardiologists, respirologists, and oncologists, discerned from surveys (the Canadian Palliative Cardiology/Respirology/Oncology Surveys).

Methods: Descriptive comparison of survey studies; multivariable linear regression analysis of association between specialty and referral frequency. Surveys for each specialty were disseminated to physicians across Canada in 2010 (oncologists) and 2018 (cardiologists, respirologists).

Results: The combined response rate of the surveys was 60.9% (1,568/2,574): 603 oncologists, 534 cardiologists, and 431 respirologists. Perceived availability of specialist palliative care services was higher for cancer than for non-cancer patients. Oncologists were more likely to make a referral to specialist palliative care for a symptomatic patient with a prognosis of <1 year. Cardiologists and respirologists were more likely to make a referral to services at a prognosis of <1 month; and to refer earlier if palliative care was renamed supportive care. Cardiologists and respirologists had a lower frequency of referral than oncologists, adjusting for demographic and professional characteristics ($p<0.0001$ in both groups).

Conclusion: For cardiologists and respirologists in 2018, perceived availability of specialist palliative care services was poorer, timing of referral later, and frequency of referral lower than among oncologists in 2010. Further research is needed to identify reasons for differences in referral practices and to develop interventions to overcome them.

Keywords: cancer; chronic obstructive pulmonary disease; health care disparity; heart failure; palliative care; referral.

Am J Respir Crit Care Med

. 2023 Feb 16.
doi: 10.1164/rccm.202207-1384OC. Online ahead of print.

A Unique Cellular Organization of Human Distal Airways and Its Disarray in Chronic Obstructive Pulmonary Disease

Samir Rustam [1], Yang Hu [1], Seyed Babak Mahjour [2], Andre F Rendeiro [2], Hiranmayi Ravichandran [2], Andreacarola Urso [3], Frank D'Ovidio [4], Fernando J Martinez [5], Nasser K Altorki [6], Bradley Richmond [7], Vasiliy Polosukhin [7], Jonathan A Kropski [7], Timothy S Blackwell [7], Scott H Randell [8], Olivier Elemento [9], Renat Shaykhiev [10]
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- PMID: 36796082

- DOI: 10.1164/rccm.202207-1384OC

Abstract

Rationale: Remodeling and loss of distal conducting airways, including pre-terminal and terminal bronchioles (pre-TB/TBs), underlie progressive airflow limitation in chronic obstructive pulmonary disease (COPD). The cellular basis of these structural changes remains unknown.

Objective: To identify biological changes in pre-TB/TBs in COPD at single-cell resolution and determine their cellular origin.

Method: We established a novel method of distal airway dissection and performed single-cell transcriptomic profiling of 111,412 cells isolated from different airway regions of 12

healthy lung donors and pre-TBs of 5 patients with COPD. Imaging CyTOF and immunofluorescence analysis of pre-TB/TBs from 24 healthy lung donors and 11 COPD subjects were performed to characterize cellular phenotypes at a tissue level. Region-specific differentiation of basal cells isolated from proximal and distal airways was studied using an air-liquid interface model.

Results: The atlas of cellular heterogeneity along the proximal-distal axis of human lung was assembled and identified region-specific cellular states, including SCGB3A2+ SFTPB+ terminal airway-enriched secretory cells (TASCs) unique to distal airways. TASCs were lost in COPD pre-TB/TBs, paralleled by loss of region-specific endothelial capillary cells, increased frequency of CD8+ T cells normally enriched in proximal airways and augmented IFN-γ signaling. Basal cells residing in pre-TB/TBs were identified as a cellular origin of TASCs. Regeneration of TASCs by these progenitors was suppressed by IFN-γ.

Conclusion: Altered maintenance of the unique cellular organization of pre-TB/TBs, including loss of the region-specific epithelial differentiation in these bronchioles, represents the cellular manifestation and likely the cellular basis of distal airway remodeling in COPD.

Keywords: bronchiole; epithelium; heterogeneity; regeneration; remodeling.

Review

J Med Internet Res

. 2023 Feb 16;25:e33185.
doi: 10.2196/33185.

Telemedical Interventions for Chronic Obstructive Pulmonary Disease Management: Umbrella Review

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Affiliations expand

- PMID: 36795479

- DOI: 10.2196/33185

Free article

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a growing epidemic, with a heavy associated economic burden. Education, physical activity, and pulmonary rehabilitation programs are important aspects of the management of COPD. These interventions are commonly delivered remotely as part of telemedicine interventions. Several systematic reviews and meta-analyses have been conducted to assess the effectiveness of these interventions. However, these reviews often have conflicting conclusions.

Objective: We aim to conduct an umbrella review to critically appraise and summarize the available evidence on telemedicine interventions for the management of COPD.

Methods: In this umbrella review, the MEDLINE, Embase, PsycINFO, and Cochrane databases were searched from inception to May 2022 for systematic reviews and meta-analyses relating to telemedicine interventions for the management of COPD. We compared odds ratios, measures of quality, and heterogeneity across different outcomes.

Results: We identified 7 systematic reviews that met the inclusion criteria. Telemedicine interventions used in these reviews were teletreatment, telemonitoring, and telesupport. Telesupport interventions significantly reduced the number of inpatient days and quality of life. Telemonitoring interventions were associated with significant reductions in respiratory exacerbations and hospitalization rates. Teletreatment showed significant effectiveness in reducing respiratory exacerbations, hospitalization rate, compliance (acceptance and dropout rate), and physical activity. Among studies that used integrated telemedicine interventions, there was a significant improvement in physical activity.

Conclusions: Telemedicine interventions showed noninferiority or superiority over the standard of care for the management of COPD. Telemedicine interventions should be considered as a supplement to usual methods of care for the outpatient management of COPD, with the aim of reducing the burden on health care systems.

Keywords: chronic obstructive pulmonary disease; telehealth; telemedicine.

Review

Interact J Med Res

. 2023 Feb 16;12:e42396.
doi: 10.2196/42396.

Cost-effectiveness of Digital Tools for Behavior Change Interventions Among People With Chronic Diseases: Systematic Review

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Affiliations expand

- PMID: 36795470
- DOI: 10.2196/42396

Free article

Abstract

Background: Chronic diseases, including cardiovascular diseases, diabetes, chronic obstructive pulmonary disease, and cerebrovascular diseases, contribute to the most significant disease burden worldwide, negatively impacting patients and their family members. People with chronic diseases have common modifiable behavioral risk factors, including smoking, alcohol overconsumption, and unhealthy diets. Digital-based interventions for promoting and sustaining behavioral changes have flourished in recent years, although evidence of the cost-effectiveness of such interventions remains inconclusive.

Objective: In this study, we aimed to investigate the cost-effectiveness of digital health interventions for behavioral changes among people with chronic diseases.

Methods: This systematic review evaluated published studies focused on the economic evaluation of digital tools for behavioral change among adults with chronic diseases. We

followed the Population, Intervention, Comparator, and Outcomes framework to retrieve relevant publications from 4 databases: PubMed, CINAHL, Scopus, and Web of Science. We used the Joanna Briggs Institute's criteria for economic evaluation and randomized controlled trials to assess the risk of bias in the studies. Two researchers independently screened, assessed the quality, and extracted data from the studies selected for the review.

Results: In total, 20 studies published between 2003 and 2021 fulfilled our inclusion criteria. All the studies were conducted in high-income countries. These studies used telephones, SMS text messaging, mobile health apps, and websites as digital tools for behavior change communication. Most digital tools for interventions focused on diet and nutrition (17/20, 85%) and physical activity (16/20, 80%), and a few focused on smoking and tobacco control (8/20, 40%), alcohol reduction (6/20, 30%), and reduction of salt intake (3/20, 15%). Most studies (17/20, 85%) used the health care payer perspective for economic analysis, and only 15% (3/20) used the societal perspective. Only 45% (9/20) of studies conducted a full economic evaluation. Most studies (7/20, 35%) based on full economic evaluation and 30% (6/20) of studies based on partial economic evaluation found digital health interventions to be cost-effective and cost-saving. Most studies had short follow-ups and failed to include proper indicators for economic evaluation, such as quality-adjusted life-years, disability-adjusted life-years, lack of discounting, and sensitivity analysis.

Conclusions: Digital health interventions for behavioral change among people with chronic diseases are cost-effective in high-income settings and can therefore be scaled up. Similar evidence from low- and middle-income countries based on properly designed studies for cost-effectiveness evaluation is urgently required. A full economic evaluation is needed to provide robust evidence for the cost-effectiveness of digital health interventions and their potential for scaling up in a wider population. Future studies should follow the National Institute for Health and Clinical Excellence recommendations to take a societal perspective, apply discounting, address parameter uncertainty, and apply a lifelong time horizon.

Keywords: behavior; chronic diseases; cost-effectiveness; digital tools; lifestyle; mobile phone; systematic review.

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Kidney360
.
. 2023 Feb 14.
doi: 10.34067/KID.0000000000000078. Online ahead of print.

Geriatric syndromes and health-related quality of life in older adults with chronic kidney disease

Christine K Liu[1 2 3], Shiyuan Miao[4], Jamie Giffuni[5], Leslie I Katzel[5 6], Roger A Fielding[3], Stephen L Seliger[5 7], Daniel E Weiner[4]
Affiliations expand

- PMID: 36790849
- DOI: 10.34067/KID.0000000000000078

Free article

Abstract

Background: Geriatric syndromes, which are multi-factorial conditions common in older adults, predict health-related quality of life (HRQOL). Although chronic kidney disease (CKD) is associated with lower HRQOL, whether geriatric syndromes contribute to HRQOL in CKD is unknown. Our objective was to compare associations of geriatric syndromes and medical conditions with HRQOL in older adults with CKD.

Methods: This was a secondary analysis of a parallel-group randomized controlled clinical trial evaluating a 12- month exercise intervention in persons ≥55 years with CKD Stage 3b-4. Participants were assessed for baseline geriatric syndromes (cognitive impairment, poor appetite, dizziness, fatigue, and chronic pain), and medical conditions (diabetes, hypertension, coronary artery disease, cancer, or chronic obstructive pulmonary disease). Participants' HRQOL was assessed with the Short Form Health Survey-36 (SF-36), EuroQol 5 Dimensions-5 Level, and the EuroQol Visual Analogue Scale. We examined the cross-sectional and longitudinal associations of geriatric syndromes and medical conditions with HRQOL using multiple linear regression.

Results: Among 99 participants, the mean age was 68.0 years, 25% were female, and 62% were Black. Participants had a baseline mean of 2.0 geriatric syndromes and 2.1 medical conditions; 49% had ≥ two geriatric syndromes and ≥ two medical conditions concurrently. Sixty-seven participants (68%) underwent 12-month assessments. In models using geriatric

syndromes and medical conditions as concurrent exposures, the number of geriatric syndromes was cross-sectionally associated with SF-36 scores for general health (β = -0.385), role limitations due to physical health (β=-0.374), physical functioning (β= -0.300, all p < 0.05). The number of medical conditions was only associated with SF-36 score for role limitations due to physical health (β = -0.205).

Conclusions: In older adults with CKD Stage 3b-4, geriatric syndromes are common and are associated with lower HRQOL. Addressing geriatric conditions is a potential approach to improve HRQOL for older adults with CKD.

Review

Lung
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. 2023 Feb 15.
doi: 10.1007/s00408-023-00607-9. Online ahead of print.

SIRT1 as a Potential Therapeutic Target for Chronic Obstructive Pulmonary Disease

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Affiliations expand

- PMID: 36790647

- DOI: 10.1007/s00408-023-00607-9

Abstract

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by irreversible airflow obstruction and lung function decline. It is well established that COPD represents a major cause of morbidity and mortality globally. Due

to the substantial economic and social burdens associated with COPD, it is necessary to discover new targets and develop novel beneficial therapies. Although the pathogenesis of COPD is complex and remains to be robustly elucidated, numerous studies have shown that oxidative stress, inflammatory responses, cell apoptosis, autophagy, and aging are involved in the pathogenesis of COPD. Sirtuin 1 (SIRT1) is a nicotinamide adenine dinucleotide (NAD+)-dependent deacetylase belonging to the silent information regulator 2 (Sir2) family. Multiple studies have indicated that SIRT1 plays an important role in oxidative stress, apoptosis, inflammation, autophagy, and cellular senescence, which contributes to the pathogenesis and development of COPD. This review aimed to discuss the functions and mechanisms of SIRT1 in the progression of COPD and concluded that SIRT1 activation might be a potential therapeutic strategy for COPD.

Keywords: Apoptosis; Autophagy; Cellular senescence; Chronic obstructive pulmonary disease; Inflammation; Oxidative stress; Sirtuin1.

12
Crit Care Med
. 2023 Feb 15.
doi: 10.1097/CCM.0000000000005807. Online ahead of print.

Management of Acute Exacerbations of Chronic Obstructive Pulmonary Disease in the ICU: An Observational Study From the OUTCOMEREA Database, 1997-2018

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Affiliations expand

- PMID: 36790209

- DOI: 10.1097/CCM.0000000000005807

Abstract

Objectives: Our aim was to describe changes in the management of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) by ICUs and patient outcomes.

Design: We extracted data from the OutcomeRea database concerning patients admitted for AECOPD between 1997 and 2018. We analyzed trends in the use of ventilatory support, corticosteroid therapy, antibiotic therapy, and patient survival.

Setting: ICUs at 32 French sites.

Patients: One thousand eight hundred sixteen patients in the database had a diagnosis of AECOPD.

Interventions: None.

Measurements and main results: Over time, there was a reduction in the prescription of corticosteroids and antibiotics. In a time-series analysis, these changes in practice were not linked with ICU mortality. The proportion of patients treated with invasive mechanical ventilation (IMV) also gradually declined (from 51% between 1997 and 2002 to 35% between 2013 and 2018) with an association between decrease in IMV use and reduction in ICU mortality in a time series analysis. Rates of noninvasive ventilation (NIV) failure decreased with an increase in NIV use to support weaning from IMV. There was a reduction in the median ICU length of stay (from 8 d in 1997-2002 to 4 d in 2013-2018) and in the median total duration of hospitalization (from 23 d in 1997-2002 to 14 d in 2013-2018). We observed an improvement in prognosis, with decreases in overall hospital mortality (from 24% between 1997 and 2002 to 15% between 2013 and 2018), ICU mortality (from 14% between 1997 and 2002 to 10% between 2013 and 2018), and 90-day mortality (from 41% between 1997 and 2002 to 22% between 2013 and 2018).

Conclusions: The length of stay and mortality of patients with AECOPD admitted to ICUs has decreased over the last 20 years, with a wider use of NIV and a reduction in antibiotic and corticosteroid prescriptions.

Conflict of interest statement

Dr. Terzi received funding from Pfizer for attending meetings and/or travel. Dr. Hong Tuan Ha disclosed work for hire. The remaining authors have disclosed that they do not have any potential conflicts of interest.

- 42 references

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PLoS One

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. 2023 Feb 14;18(2):e0281715.
doi: 10.1371/journal.pone.0281715. eCollection 2023.

Lobar emphysema ratio of more than 1% in the lobe with lung cancer as poor predictor for recurrence and overall survival in patients with stage I non-small cell lung cancer

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Affiliations expand

- PMID: 36787324
- PMCID: PMC9928128
- DOI: 10.1371/journal.pone.0281715

Free PMC article

Abstract

Background: The purpose of this study was to examine the relationship between the lobar emphysema ratio (LER) and tumor recurrence and survival in patients with stage I non-small cell lung cancer (NSCLC).

Methods: We enrolled 258 patients with surgically proven stage I NSCLC. These patients underwent noncontrast chest CT, and pulmonary lobe segmentation and lobar emphysema quantification were performed using commercially available software. We assessed the LER in the lobe with lung cancer. We divided the patients into two groups according to the LER, and the cut-off value was 1. Furthermore, we analyzed the disease-free survival of high LER and other clinical factors after surgical resection.

Results: The 258 patients were divided into two groups: low LER (n = 195) and high LER (n = 63). The right upper lobe was the most frequent location in lung cancer and the most severe location in emphysema. In the Kaplan–Meier curve, high LER showed a significantly lower disease-free survival (8.21 ± 0.27 years vs 6.53 ± 0.60 years, p = 0.005) and overall survival (9.56 ± 0.15 years vs. 8.51 ± 0.49 years, p = 0.011) than low LER. Stage Ib (2.812 [1.661-4.762], p<0.001) and high LER (2.062 [1.191-3.571], p = 0.010) were poor predictors for disease-free survival in multivariate Cox regression analysis. Stage Ib (4.729 [1.674-13.356], p = 0.003) and high LER (3.346 [1.208-9.269], p = 0.020) were significant predictors for overall survival in multivariate Cox regression analysis.

Conclusion: A LER of more than 1% in the lobe with lung cancer is a poor predictor for cancer recurrence and overall survival in patients with stage I NSCLC.

Conflict of interest statement

The authors have declared that no competing interests exist.

- 31 references
- 2 figures

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JAMA

. 2023 Feb 14;329(6):490-501.
doi: 10.1001/jama.2023.0128.

Discriminative Accuracy of the CAPTURE Tool for Identifying Chronic Obstructive Pulmonary Disease in US Primary Care Settings

Fernando J Martinez[1], MeiLan K Han[2], Camden Lopez[3], Susan Murray[3], David Mannino[4], Stacey Anderson[3], Randall Brown[3], Rowena Dolor[5], Nancy Elder[6], Min Joo[7], Irfan Khan[8], Lyndee M Knox[9], Catherine Meldrum[2], Elizabeth Peters[1], Cathie Spino[3], Hazel Tapp[10], Byron Thomashow[11], Linda Zittleman[12], Barry Make[13], Barbara P Yawn[14]; CAPTURE Study Group
Collaborators, Affiliations expand

- PMID: 36786790
- PMCID: PMC9929696 (available on 2023-08-14)
- DOI: 10.1001/jama.2023.0128

Abstract

Importance: Chronic obstructive pulmonary disease (COPD) is underdiagnosed in primary care.

Objective: To evaluate the operating characteristics of the CAPTURE (COPD Assessment in Primary Care To Identify Undiagnosed Respiratory Disease and Exacerbation Risk) screening tool for identifying US primary care patients with undiagnosed, clinically significant COPD.

Design, setting, and participants: In this cross-sectional study, 4679 primary care patients aged 45 years to 80 years without a prior COPD diagnosis were enrolled by 7 primary care practice-based research networks across the US between October 12, 2018, and April 1, 2022. The CAPTURE questionnaire responses, peak expiratory flow rate, COPD Assessment Test scores, history of acute respiratory illnesses, demographics, and spirometry results were collected.

Exposure: Undiagnosed COPD.

Main outcomes and measures: The primary outcome was the CAPTURE tool's sensitivity and specificity for identifying patients with undiagnosed, clinically significant COPD. The secondary outcomes included the analyses of varying thresholds for defining a positive screening result for clinically significant COPD. A positive screening result was defined as (1) a CAPTURE questionnaire score of 5 or 6 or (2) a questionnaire score of 2, 3, or 4 together with a peak expiratory flow rate of less than 250 L/min for females or less than 350 L/min for males. Clinically significant COPD was defined as spirometry-defined COPD (postbronchodilator ratio of forced expiratory volume in the first second of expiration [FEV1] to forced vital capacity [FEV1:FVC] <0.70 or prebronchodilator FEV1:FVC <0.65 if postbronchodilator spirometry was not completed) combined with either an FEV1 less than 60% of the predicted value or a self-reported history of an acute respiratory illness within the past 12 months.

Results: Of the 4325 patients who had adequate data for analysis (63.0% were women; the mean age was 61.6 years [SD, 9.1 years]), 44.6% had ever smoked cigarettes, 18.3% reported a prior asthma diagnosis or use of inhaled respiratory medications, 13.2% currently smoked cigarettes, and 10.0% reported at least 1 cardiovascular comorbidity. Among the 110 patients (2.5% of 4325) with undiagnosed, clinically significant COPD, 53 had a positive screening result with a sensitivity of 48.2% (95% CI, 38.6%-57.9%) and a specificity of 88.6% (95% CI, 87.6%-89.6%). The area under the receiver operating curve for varying positive screening thresholds was 0.81 (95% CI, 0.77-0.85).

Conclusions and relevance: Within this US primary care population, the CAPTURE screening tool had a low sensitivity but a high specificity for identifying clinically significant COPD defined by presence of airflow obstruction that is of moderate severity or accompanied by a history of acute respiratory illness. Further research is needed to optimize performance of the screening tool and to understand whether its use affects clinical outcomes.

Conflict of interest statement

Conflict of Interest Disclosures: Dr Martinez reported receiving grants from Chiesi Farmaceutici, CSL Behring, GSK (formerly GlaxoSmithKline), Medtronic, Novartis, Polarean, Sanofi, and Regeneron; receiving personal fees from AstraZeneca, Boehringer Ingelheim, GSK, Polarean, Pulmatrix, Sanofi, Regeneron, Theravance Biopharma, and Viatris; receiving travel reimbursement from AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, CSL Behring, and GSK; and having a patent for the CAPTURE screening tool that is licensed to Weill Cornell Medicine. Dr Han reported receiving personal fees from GSK, AstraZeneca, Verona Pharma, Merck, MDBriefCase, Mylan (now part of Viatris), DevPro Biopharma, Aerogen, Polarean, Regeneron, UpToDate, Altesa BioSciences, Medscape, Integrity, Boehringer Ingelheim, Cipla, Chiesi Farmaceutici, Novartis, Pulmonx, Teva Pharmaceuticals, and the National Association for Continuing Education; receiving grants from the American Lung Association, AstraZeneca, Boehringer Ingelheim, the COPD Foundation, Biodesix, Gala Therapeutics, Medtronic, Sanofi, Sunovion, and Nuvaira Inc; and having stock options in Altesa BioSciences and Meissa Vaccines. Dr Mannino reported receiving personal fees from GSK, AstraZeneca, UpToDate, and Schlesinger law firm. Dr Brown reported receiving

personal fees from Teva Pharmaceuticals. Dr Khan reported being the CEO and receiving standard clinical trial site and enrollment fees for study execution paid to Circuit Clinical (employer and clinical trials company). Dr Spino reported receiving grants from the Three Lakes Foundation. Dr Thomashow reported receiving personal fees from GSK, Boehringer Ingelheim, and Reckitt Health and being the co-founder and chief medical officer (volunteer position) of the COPD Foundation, which is a nonprofit organization. Dr Make reported receiving grants from the American Lung Association and the US Department of Defense; receiving personal fees from the American College of Chest Physicians, AstraZeneca, GSK, Integritas, Boehringer Ingelheim, Mylan, Novartis, Optimum Patient Care Global, Projects in Knowledge, IQVIA (formerly Quintiles and IMS Health), Third Pole, University of Wisconsin, WebMD, and Mt Sinai; and having a patent and receiving royalties from Wolters Kluwer Health (UpToDate). Dr Yawn reported receiving personal fees from GSK, Teva Pharmaceuticals, AstraZeneca, and Boehringer Ingelheim. No other disclosures were reported.

Comment in

- doi: 10.1001/jama.2021.23255

supplementary info

Publication types, MeSH terms, Grant supportexpand

full text links

Med Sci Monit

. 2023 Feb 14;29:e938554.
doi: 10.12659/MSM.938554.

Association Between Neutrophil-Lymphocyte Ratio and All-Cause Mortality in Critically Ill Patients with Chronic Obstructive Pulmonary Disease: A Retrospective Cohort Study

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Affiliations expand
- PMID: 36785492
- PMCID: PMC9938631
- DOI: 10.12659/MSM.938554

Abstract

BACKGROUND Neutrophil-lymphocyte ratio (NLR) is related to increased mortality risk in many diseases. However, there is limited research on critically ill patients with chronic obstructive pulmonary disease (COPD). A retrospective cohort study was performed to investigate whether NLR can be used as a biomarker to predict the mortality of critically ill COPD patients. MATERIAL AND METHODS In the research, the data were gathered from the database of the Medical Information Mart for Intensive Care-IV. The 28-day mortality was defined as the primary outcome, while the secondary outcomes were in-hospital and 90-day mortality. Through the application of the Kaplan-Meier curves and the multivariate Cox regression analysis, the potential association between NLR and mortality for critically ill patients with COPD was evaluated. For subgroup analysis, age, sex, ethnicity, mean blood pressure, and comorbidities were considered. RESULTS We extracted data on 2650 patients, of which 53.7% were male. A higher level of NLR was correlated with higher 28-day mortality risk. Compared to the lower quartile (NLR<4.56), HR (95% CI) of the upper quartile (NLR>16.86) was 1.75 (1.21-2.52) in the multivariate Cox regression model when adjusted for confounders (P=0.003). A similar tendency was found in the 90-day mortality (HR=1.59, 95% CI=1.16-2.19, P=0.004) and the in-hospital mortality (HR=1.71, 95% CI=1.22-2.42, P=0.002). Subgroup analyses showed that the correlation between NLR and 28-day mortality was stable. CONCLUSIONS The higher level of NLR is likely to be correlated with the increase of the all-cause mortality risk in critically ill patients with COPD, but this needs to be validated in future prospective research.

Conflict of interest statement

Conflict of interest: None declared

- 50 references
- 2 figures

supplementary info

MeSH termsexpand

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Am J Respir Cell Mol Biol
.
. 2023 Feb 13.
doi: 10.1165/rcmb.2022-0302OC. Online ahead of print.

Integrating Genetics, Transcriptomics, and Proteomics in Lung Tissue to Investigate COPD

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- PMID: 36780661
- DOI: 10.1165/rcmb.2022-0302OC

Abstract

The integration of transcriptomic and proteomic data from lung tissue with chronic obstructive pulmonary disease (COPD)-associated genetic variants could provide insight into the biological mechanisms for COPD. Here, we assessed associations between lung transcriptomics and proteomics with COPD in 98 subjects from the Lung Tissue Research Consortium. Low correlations between transcriptomics and proteomics were generally observed, but higher correlations were found for COPD-associated proteins. We integrated COPD risk SNPs or SNPs near COPD-associated proteins with lung transcripts and proteins to identify regulatory cis quantitative trait loci (QTLs). Significant expression QTLs (eQTLs) and protein QTLs (pQTLs) were found regulating multiple COPD-associated biomarkers. We investigated mediated associations from significant protein quantitative trait loci through transcripts to protein levels of COPD-associated proteins. We also attempted to identify colocalized effects between GWAS, eQTL, and pQTL signals. Evidence for colocalization between COPD GWAS signals and pQTL for RHOB and eQTL for DSP was found. We applied Weighted Gene Co-Expression Network Analysis (WGCNA) to find consensus COPD-associated network modules. Two network modules generated by consensus WGCNA were associated with COPD with FDR < 0.05. One network module is related to the catenin complex, and the other module is related to plasma membrane components. In summary, multiple cis-acting effects for transcripts and proteins associated with COPD were identified. Colocalization analysis, mediation analysis, and correlation-based network analysis of multiple Omics data may identify key genes and proteins that work together to influence COPD pathogenesis.

Keywords: chronic obstructive pulmonary disease; multi-Omics analyses; quantitative trait locus; weighted gene co-expression network analysis.

Int J Epidemiol

. 2023 Feb 13;dyad011.
doi: 10.1093/ije/dyad011. Online ahead of print.

Associations between serum high-density lipoprotein cholesterol levels and cause-specific mortality in a general population of 345 000 men and women aged 20-79 years

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Affiliations expand

- PMID: 36779319
- DOI: 10.1093/ije/dyad011

Abstract

Background: Benefits of elevated high-density lipoprotein cholesterol (HDL-C) levels are challenged by reports demonstrating U-shaped relations between HDL-C levels and all-cause mortality; the association with cause-specific mortality is less studied.

Methods: A total of 344 556 individuals (20-79 years, 52 % women) recruited from population-based health screening during 1985-2003 were followed until the end of 2018 for all-cause and cause-specific mortality by serum HDL-C level at inclusion of <30, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90-99 and >99 mg/dl (< 0.78, 0.78-1.01, 1.04-1.27, 1.30-1.53, 1.55-1.79, 1.81-2.04, 2.07-2.31, 2.33-2.56, >2.56 mmol/L). Hazard ratios (HRs) were

adjusted for sex, age, calendar period, smoking, total cholesterol, triglycerides, systolic blood pressure, physical activity, educational length, body mass index and ill health.

Results: During a mean follow-up of 22 years, 69 505 individuals died. There were U-shaped associations between HDL-C levels and all-cause, cancer and non-cardiovascular disease/non-cancer mortality (non-CVD/non-cancer), whereas for CVD there was increased risk of death only at lower levels. With HDL-C stratum 50-59 mg/dl (1.30-1.53 mmol/L) as reference, HRs [95% confidence intervals (CIs)] for levels >99 mg/dl (>2.56 mmol/L) were 1.32 (1.21-1.43), 1.05 (0.89-1.24), 1.26 (1.09-1.46) and 1.68 (1.48-1.90) for all-cause, CVD, cancer and non-CVD/non-cancer mortality, respectively. For HDL-C levels <30 mg/dl (0.78 mmol/L), the corresponding HRs (95% CIs) were 1.30 (1.24-1.36), 1.55 (1.44-1.67), 1.14 (1.05-1.23) and 1.19 (1.10-1.29). The mortality from alcoholic liver disease, cancers of mouth-oesophagus-liver, chronic liver diseases, chronic obstructive pulmonary disease, accidents and diabetes increased distinctly with increasing HDL-C above the reference level. HDL-C levels lower than the reference level were mainly associated with increased mortality of ischaemic heart disease (IHD), other CVDs, stomach cancer and diabetes.

Conclusions: Higher HDL-C levels were associated with increased mortality risk of several diseases which also have been associated with heavy drinking, and lower HDL-C levels were associated with increased mortality from IHD, other CVDs, gastric cancer and diabetes.

Keywords: High-density lipoprotein cholesterol (HDL-C); epidemiology; general population; mortality.

Microbiol Spectr

. 2023 Feb 14;11(1):e0386022.
doi: 10.1128/spectrum.03860-22. Epub 2022 Dec 8.

Genetic Adaptation and Acquisition of Macrolide Resistance in Haemophilus

spp. during Persistent Respiratory Tract Colonization in Chronic Obstructive Pulmonary Disease (COPD) Patients Receiving Long-Term Azithromycin Treatment

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Affiliations expand

- PMID: 36475849
- PMCID: PMC9927455
- DOI: 10.1128/spectrum.03860-22

Free PMC article

Abstract

Patients with chronic obstructive pulmonary disease (COPD) benefit from the immunomodulatory effect of azithromycin, but long-term administration may alter colonizing bacteria. Our goal was to identify changes in Haemophilus influenzae and Haemophilus parainfluenzae during azithromycin treatment. Fifteen patients were followed while receiving prolonged azithromycin treatment (Hospital Universitari de Bellvitge, Spain). Four patients (P02, P08, P11, and P13) were persistently colonized by H. influenzae for at least 3 months and two (P04 and P11) by *H. parainfluenzae*. Isolates from these patients (53 H. influenzae and 18 *H. parainfluenzae*) were included to identify, by whole-genome sequencing, antimicrobial resistance changes and genetic variation accumulated during persistent colonization. All persistent lineages isolated before treatment were azithromycin-susceptible but developed resistance within the first months, apart from those belonging to P02, who discontinued the treatment. H. influenzae isolates from P08-ST107 acquired mutations in 23S rRNA, and those from P11-ST2480 and P13-ST165 had changes in L4 and L22. In *H. parainfluenzae*, P04 persistent isolates acquired changes in *rlmC*, and P11 carried genes encoding MefE/MsrD efflux pumps in an integrative conjugative element, which was also identified in H. influenzae P11-ST147. Other genetic variation occurred in genes associated with cell wall and inorganic ion metabolism. Persistent H. influenzae strains all showed changes in *licA* and *hgpB* genes. Other genes (*lex1*, *lic3A*, *hgpC*, and *fadL*) had variation in multiple lineages. Furthermore, persistent strains showed loss, acquisition, or genetic changes in prophage-associated regions. Long-

term azithromycin therapy results in macrolide resistance, as well as genetic changes that likely favor bacterial adaptation during persistent respiratory colonization. **IMPORTANCE** The immunomodulatory properties of azithromycin reduce the frequency of exacerbations and improve the quality of life of COPD patients. However, long-term administration may alter the respiratory microbiota, such as Haemophilus influenzae, an opportunistic respiratory colonizing bacteria that play an important role in exacerbations. This study contributes to a better understanding of COPD progression by characterizing the clinical evolution of H. influenzae in a cohort of patients with prolonged azithromycin treatment. The emergence of macrolide resistance during the first months, combined with the role of Haemophilus parainfluenzae as a reservoir and source of resistance dissemination, is a cause for concern that may lead to therapeutic failure. Furthermore, genetic variations in cell wall and inorganic ion metabolism coding genes likely favor bacterial adaptation to host selective pressures. Therefore, the bacterial pathoadaptive evolution in these severe COPD patients raise our awareness of the possible spread of macrolide resistance and selection of host-adapted clones.

Keywords: Haemophilus influenzae; Haemophilus parainfluenzae; adaptation; azithromycin; macrolide resistance; persistence.

Conflict of interest statement

The authors declare no conflict of interest.

Am J Respir Crit Care Med

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. 2023 Feb 15;207(4):495-496.
doi: 10.1164/rccm.202210-1877LE.

Efficacy of High-Flow Nasal Cannula Oxygen Therapy in Reducing Future

Exacerbations for Patients with Stable Hypercapnia with Chronic Obstructive Pulmonary Disease

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Affiliations expand

- PMID: 36346704

- DOI: 10.1164/rccm.202210-1877LE

No abstract available

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Publication types, MeSH terms, Substances, Grant supportexpand

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Case Reports

Occup Med (Lond)

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. 2023 Feb 14;73(1):49-52.
doi: 10.1093/occmed/kqac111.

Acute exacerbation of chronic obstructive pulmonary disease in a slaughterhouse

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Affiliations expand

- PMID: 36282619

- DOI: 10.1093/occmed/kqac111

Abstract

We describe the case of a 52-year-old male who presented with two episodes of acute exacerbations (AE) of chronic obstructive pulmonary disease (COPD) during work, while suspending live chickens for slaughter. The patient was exposed to high levels of bioaerosols, including endotoxins and microorganisms. Endotoxins can induce bronchoconstriction and airway inflammation, and COPD patients are more vulnerable to airway infections caused by microorganisms inhaled with bioaerosols. This study suggests that a high level of bioaerosols may induce airway infections, resulting in acute exacerbations of COPD.

ASTHMA

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PLoS One

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. 2023 Feb 17;18(2):e0281923.

doi: 10.1371/journal.pone.0281923. eCollection 2023.

Asthma and its relationship with anthropometric markers among adults

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Affiliations expand

- PMID: 36800359
- PMCID: PMC9937501
- DOI: 10.1371/journal.pone.0281923

Abstract

Background: Many studies have examined the association between anthropometric indicators and the likelihood of developing asthma. However, no study has yet examined the link between asthma and anthropometric markers of risk. This study addresses this gap in the literature by evaluating the relationship between asthma, smoking, and anthropometric measurements such as body mass index (BMI), waist circumference (WC), hip circumference (HC), and waist-to-hip ratio (WHR) among individuals residing in the United States.

Methods: This cross-sectional study conducted a secondary analysis of the 2011-2014 National Survey of Midlife Development in the United States, using data from 2,257 participants aged 25-74. We classified the participants into four groups based on self-reported smoking and asthma status: nonsmokers with no asthma, asthma alone, smokers only, and smokers with asthma. The outcomes of interest were BMI, WC, HC, and WHR scores in the latter three groups compared to the nonsmokers with no asthma group.

Results: Linear regression analysis showed that those with asthma alone and smokers with asthma were significantly more likely to have a BMI, WC, or HC score of 1 or higher than people without asthma and smokers only.

Conclusion: A higher score on the anthropometric parameters was substantially related to participants who had only asthma and those who had both asthma and smoking.

Conflict of interest statement

The authors have declared that no competing interests exist.

- 35 references
- 1 figure

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Review

Allergy

. 2023 Feb 17.
doi: 10.1111/all.15679. Online ahead of print.

Rhinitis associated with asthma is distinct from rhinitis alone: The ARIA-MeDALL hypothesis

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Ohta[209], K Okubo[210], S Ouedraogo[211], H Olze[212], I Pali-Schöll[213], O Palomares[214], K Palosuo[215], C Panaitescu[216], P Panzner[217], H S Park[218], C Pitsios[219], D Plavec[220], T A Popov[221], F Puggioni[30], S Quirce[222], M Recto[223], R Repka-Ramirez[224], C Roballo-Cordeiro[225], N Roche[226,227], M Rodriguez-Gonzales[228], J Romantowski[63], N Rosario Filho[229], M Rottem[230], H Sagara[231], F Sarquis-Serpa[232], Z Sayah[233], S Scheire[234], P Schmid-Grendelmeier[235], J C Sisul[236], D Sole[237], M Soto-Martinez[238], M Sova[239], A Sperl[46], O Spranger[240], R Stelmach[241], C Suppli Ulrik[242], M Thomas[243], T To[244], A Todo-Bom[245], P V Tomazic[246], M Urrutia-Pereira[247], M Valentin-Rostan[248], E van Ganse[249], M Van Hage[250], T Vasankari[251,252], P Vichyanond[253], G Viegi[254], D Wallace[255], D Y Wang[256], S Williams[96], M Worm[257], P Yiallouros[219], P Yiallouros[219], O Yusuf[258], F Zaitoun[259], M Zernotti[260], M Zidarn[261,262], J Zuberbier[212], J A Fonseca[87,88,89], T Zuberbier[1,2], J M Anto[28,29,91,92]
Affiliations expand

- PMID: 36799120

- DOI: 10.1111/all.15679

Abstract

Asthma, rhinitis and atopic dermatitis (AD) are interrelated clinical phenotypes that partly overlap in the human interactome. The concept of "one-airway-one-disease", coined over 20 years ago, is a simplistic approach of the links between upper- and lower-airway allergic diseases. With new data, it is time to reassess the concept. This article reviews (i) the clinical observations that led to Allergic Rhinitis and its Impact on Asthma (ARIA), (ii) new insights into polysensitisation and multimorbidity, (iii) advances in mHealth for novel phenotype definition, (iv) confirmation in canonical epidemiologic studies, (v) genomic findings, (vi) treatment approaches and (vii) novel concepts on the onset of rhinitis and multimorbidity. One recent concept, bringing together upper- and lower-airway allergic diseases with skin, gut and neuropsychiatric multimorbidities, is the "Epithelial Barrier Hypothesis". This review determined that the "one-airway-one-disease" concept does not always hold true and that several phenotypes of disease can be defined. These phenotypes include an extreme "allergic" (asthma) phenotype combining asthma, rhinitis and conjunctivitis. Rhinitis alone and rhinitis and asthma multimorbidity represent two distinct diseases with the following differences: (i) genomic and transcriptomic background (Toll-Like Receptors and IL-17 for rhinitis alone as a local disease; IL-33 and IL-5 for allergic and non-allergic multimorbidity as a systemic disease), (ii) allergen sensitisation patterns (mono- or pauci-sensitisation versus polysensitisation), (iii) severity of symptoms and (iv) treatment response. In conclusion, rhinitis alone (local disease) and rhinitis with asthma multimorbidity (systemic disease) should be considered as two distinct diseases, possibly modulated by the microbiome, and may be a model for understanding the epidemics of chronic and auto-immune diseases.

Keywords: IL-17; IL-33; Toll-like receptors; asthma; microbiome; multimorbidity; rhinitis.

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Respir Med

. 2023 Feb 14;107154.

doi: 10.1016/j.rmed.2023.107154. Online ahead of print.

Small airway dysfunction in asthmatic patients treated with as-needed SABA monotherapy: A perfect storm

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Affiliations expand

- PMID: 36796546
- DOI: 10.1016/j.rmed.2023.107154

Abstract

Background: Short-acting beta agonist (SABA)-only treatment is associated with poor asthma control and adverse clinical outcomes. The importance of small airway dysfunction (SAD) is increasingly recognized in asthma, but less is known in patients using SABA-only therapy. We aimed to investigate the impact of SAD on asthma control in an unselected cohort of 60 adults with physician-diagnosed intermittent asthma treated with as-needed SABA monotherapy.

Methods: All patients underwent standard spirometry and impulse oscillometry (IOS) at the first visit and were stratified by the presence of SAD defined by IOS (fall in resistance 5-20 Hz [R5-R20]>0.07 kPa × s*L^{-1}). Univariable and multivariable analyses were used to analyze cross-sectional relationships between clinical variables and SAD.

Results: SAD was present in 73% of the cohort. Compared with patients without SAD, adults with SAD had a higher number of severe exacerbations (65.9% versus 25.0%, $p < 0.05$), higher use of annual SABA canisters (median (IQR), 3 (1.75-3) versus 1 (1-2), $p < 0.001$), and significantly less well-controlled asthma (11.7% versus 75.0%, $p < 0.001$).

Spirometry parameters were similar between patients with IOS-defined SAD and those without SAD. The multivariable logistic regression analysis showed that exercise-induced bronchoconstriction symptoms (EIB, odds ratio [OR] 31.2; 95%CI:4.85-365) and night awakenings due to asthma (OR 30.3; 95%CI:2.61-1141) were independent predictors of SAD, with a high predictive power of the model incorporating these baseline predictors (AUC 0.92).

Conclusions: EIB and nocturnal symptoms are strong predictors of SAD in asthmatic patients using as-needed SABA-monotherapy, helping to distinguish subjects with SAD among patients with asthma when IOS cannot be performed.

Keywords: Asthma; Impulse oscillometry; Short-acting beta agonist; Small airways.

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.

4

Int Arch Allergy Immunol

. 2023 Feb 16;1-9.

doi: 10.1159/000528987. Online ahead of print.

Prevalence and Clinical Characteristics of Patients with Moderate-to-Severe Asthma in Japan Using a JMDC Claims Database

Dong Wang[1], Chie Ito[1,2], Yuji Homma[2], Michinori Arimitsu[2], Hajime Yoshisue[1]

Affiliations expand

- PMID: 36796345

- DOI: 10.1159/000528987

Abstract

Introduction: Although the prevalence and burden of asthma are continuously increasing, there is a lack of evidence on the landscape of moderate-to-severe asthma in Japan. Here, we report the prevalence of moderate-to-severe asthma and describe patient's demographics and clinical characteristics from 2010 to 2019 using the JMDC claims database.

Methods: Patients (≥12 years) from the JMDC database with ≥2 asthma diagnoses in 2 different months in each index year were stratified as moderate-to-severe asthma based on the definition of asthma prevention and management guideline (Japanese Guidelines for Asthma, JGL) or Global Initiative for Asthma (GINA).

Primary objective: 10-year trend (2010-2019) in the prevalence of moderate-to-severe asthma.

Secondary objective: Demographics and clinical characteristics of patients from 2010 to 2019.

Results: Of 7,493,027 patients from the JMDC database, 38,089 and 133,557 were included in JGL and GINA cohorts, respectively, by 2019. Both cohorts presented an increasing trend in the prevalence rate of moderate-to-severe asthma from 2010 to 2019, irrespective of age groups. Demographics and clinical characteristics were consistent across the cohorts in each calendar year. Majority of patients were in the age group of 18-60 years in both JGL (86.6%) and GINA (84.2%) cohorts. Allergic rhinitis was the most frequent comorbidity and anaphylaxis the least frequent comorbidity reported in both the cohorts.

Conclusions: In Japan, the prevalence rate of patients with moderate-to-severe asthma, as per JGL or GINA in the JMDC database, increased from 2010 to 2019. The demographics and clinical characteristics were similar in both cohorts over the assessment duration.

Keywords: Asthma; Claims database; Clinical characteristics; Demographics; Prevalence.

. 2023 Feb 16.
doi: 10.1165/rcmb.2023-0023ED. Online ahead of print.

Early-Life Dysbiosis and Th17 Asthma: Never Is Better than Late

Dermot A Linden[1,2], Gisli G Einarsson[3]
Affiliations expand

- PMID: 36796087

- DOI: 10.1165/rcmb.2023-0023ED

No abstract available

Keywords: bronchial hyperreactivity; dysbiosis; interleukin-17; neonate.

Acta Paediatr

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. 2023 Feb 16.
doi: 10.1111/apa.16710. Online ahead of print.

Blood eosinophils during bronchiolitis were not associated with adult asthma in a Norwegian cohort study

Karen Galta Sørensen[1,2], Knut Øymar[1,2], Thomas Halvorsen[2,3], Ingvild Bruun Mikalsen[1,2]
Affiliations expand

- PMID: 36794990

- DOI: 10.1111/apa.16710

No abstract available

Review

Cell Biochem Funct

. 2023 Feb 16.
doi: 10.1002/cbf.3780. Online ahead of print.

Macrophage efferocytosis in health and disease

Shokufeh Razi[1], Javad Yaghmoorian Khojini[2], Fateme Kargarijam[3], Susan Panahi[4], Zahra Tahershamsi[5], Amir Tajbakhsh[6 7], Seyed Mohammad Gheibihayat[2 8]
Affiliations expand

- PMID: 36794573

- DOI: 10.1002/cbf.3780

Abstract

Creating cellular homeostasis within a defined tissue typically relates to the processes of apoptosis and efferocytosis. A great example here is cell debris that must be removed to prevent unwanted inflammatory responses and then reduce autoimmunity. In view of that, defective efferocytosis is often assumed to be responsible for the improper clearance of apoptotic cells (ACs). This predicament triggers off inflammation and even results in disease development. Any disruption of phagocytic receptors, molecules as bridging groups, or signaling routes can also inhibit macrophage efferocytosis and lead to the impaired clearance of the apoptotic body. In this line, macrophages as professional phagocytic cells take the lead in the efferocytosis process. As well, insufficiency in macrophage efferocytosis facilitates the spread of a wide variety of diseases, including neurodegenerative diseases, kidney problems, types of cancer, asthma, and the like. Establishing the functions of macrophages in this respect can be thus useful in the treatment of many diseases. Against this background, this review aimed to recapitulate the

knowledge about the mechanisms related to macrophage polarization under physiological or pathological conditions, and shed light on its interaction with efferocytosis.

Keywords: M1/M2 polarization; apoptotic cell clearance; efferocytosis; inflammation; macrophage polarization.

- 157 references

supplementary info

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Eur J Immunol
.
. 2023 Feb 15;e2250101.
doi: 10.1002/eji.202250101. Online ahead of print.

Airway epithelial type-2 alarmin profiles: Blood eosinophil counts remain in memory

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Affiliations expand

- PMID: 36793156

- DOI: 10.1002/eji.202250101

Abstract

Epithelial cytokines are involved in the orchestration of T1/T2 inflammatory patterns. We question the persistence of this trait in air-liquid interface epithelial cultures (ALI) and whether this local orientation can be related to systemic patterns (e.g. blood eosinophil counts (BECs). We investigated alarmin release related to high-vs-low T2 phenotypes associated with chronic airway diseases. ALIs were reconstituted from 32 control, 40 chronic obstructive pulmonary disease (COPD) and 20 asthmatic patients. Interleukin-8 (IL-

8; a T1-cytokine), IL-25, IL-33 and Thymic Stromal Lymphopoietin (TSLP)(T2-alarmins) concentrations were assessed in subnatants at steady state, and used to explain blood neutrophil and eosinophil counts. IL-25 and IL-8 levels were highest in asthma ALI-subnatants, whereas IL-33 was sparsely detected. TSLP levels were similar among groups. All asthma cell cultures were T1-high/T2-high, while COPD and controls tended to be mixed. BECs were independently explained by both disease and in-culture T2-alarmin levels, irrespective of the T2-alarmin considered. The epithelial ALI-T2 signature was more frequently high in patients with a BEC>300/mm^3 . Despite removal from an in vivo environment for ≥2 months, ALIs release disease-specific cytokine "cocktails" into their subnatants, suggesting continued persistence of alarmin orientation in differentiated cell-line environments.

Keywords: IL-25; TSLP; alarmins; blood eosinophil counts; epithelial cells.

9
Virol J

. 2023 Feb 15;20(1):30.
doi: 10.1186/s12985-023-01990-8.

IL-17A plays a critical role in RSV infection in children and mice

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Affiliations expand

- PMID: 36793128
- PMCID: PMC9930016
- DOI: 10.1186/s12985-023-01990-8

Free PMC article

Abstract

Background: IL-17A is a pleiotropic cytokine and intimately associated with asthma, but its role in respiratory syncytial virus (RSV) infection is conflicting in the literature.

Methods: Children hospitalized in the respiratory department with RSV infection during RSV pandemic season of 2018-2020 were included. Nasopharyngeal aspirates were collected for pathogen and cytokines determination. In the murine model, RSV intranasal administrations were performed in wild-type and IL-17A-/- mice. Leukocytes and cytokines in bronchoalveolar lavage fluid (BALF), lung histopathology, and airway hyperresponsiveness (AHR) were measured. RORγt mRNA and IL-23R mRNA were semi-quantified by qPCR.

Results: IL-17A increased significantly in RSV-infected children and was positively associated with pneumonia severity. In the murine model, IL-17A significantly increased in BALF of mice with RSV infection. Airway inflammation, lung tissue damage and AHR were significantly alleviated in wild-type mice following IL-17A neutralization and in the IL-17A-/- mice. IL-17A decreased by removing $CD4^+$ T cells but increased by depleting $CD8^+$ T cells. IL-6, IL-21, RORγt mRNA and IL-23R mRNA dramatically increased in parallel with the rise of IL-17A.

Conclusions: IL-17A contributes to the airway dysfunctions induced by RSV in children and murine. $CD3^+CD4^+$T cells are its major cellular sources and the IL-6/IL-21-IL-23R-RORγt signaling pathway might participate in its regulation.

Keywords: Airway inflammation; IL-17A; Respiratory syncytial virus.

Conflict of interest statement

The authors declare no competing interests.

- 31 references
- 6 figures

supplementary info

MeSH terms, Substances, Grant supportexpand

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Environ Res
.
2023 Feb 13;115455.
doi: 10.1016/j.envres.2023.115455. Online ahead of print.

Relationship of long-term air pollution exposure with asthma and rhinitis in Italy: an innovative multipollutant approach

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Affiliations expand

- PMID: 36791835
- DOI: 10.1016/j.envres.2023.115455

Abstract

Background: air pollution is a complex mixture; novel multipollutant approaches could help understanding the health effects of multiple concomitant exposures to air pollutants.

Aim: to assess the relationship of long-term air pollution exposure with the prevalence of respiratory/allergic symptoms and diseases in an Italian multicenter study using single and multipollutant approaches.

Methods: 14420 adults living in 6 Italian cities (Ancona, Pavia, Pisa, Sassari, Turin, Verona) were investigated in 2005-2011 within 11 different study cohorts. Questionnaire information about risk factors and health outcomes was collected. Machine learning derived mean annual concentrations of PM_{10}, $PM_{2.5}$, NO_2 and mean summer concentrations of O_3 (μg/m^3) at residential level (1-km resolution) were used for the period 2013-2015. The associations between the four pollutants and respiratory/allergic symptoms/diseases were assessed using two approaches: a) logistic regression models (single-pollutant models), b) principal component logistic regression models (multipollutant models). All the models were adjusted for age, sex, education level, smoking habits, season of interview, climatic index and included a random intercept for cohorts.

Results: the three-year average (± standard deviation) pollutants concentrations at residential level were: 20.3 ± 6.8 μg/m^3 for $PM_{2.5}$, 29.2 ± 7.0 μg/m^3 for PM_{10}, 28.0 ± 11.2 μg/m^3 for NO_2, and 70.9 ± 4.3 μg/m^3 for summer O_3. Through the multipollutant models

the following associations emerged: PM_{10} and $PM_{2.5}$ were related to 14-25% increased odds of rhinitis, 23-34% of asthma and 30-33% of night awakening; NO_2 was related to 6-9% increased odds of rhinitis, 7-8% of asthma and 12% of night awakening; O_3 was associated with 37% increased odds of asthma attacks. Overall, the Odds Ratios estimated through the multipollutant models were attenuated when compared to those of the single-pollutant models.

Conclusions: this study enabled to obtain new information about the health effects of air pollution on respiratory/allergic outcomes in adults, applying innovative methods for exposure assessment and multipollutant analyses.

Keywords: Adults; Air pollutants; Asthma; Multipollutant approach; Observational study; Rhinitis.

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: Maria Beatrice Bilò had speaking and lecture fees supported by Astra Zeneca, GSK, Novartis, Sanofi. The other authors have no competing financial interests or personal relationships to disclose.

mSystems

. 2023 Feb 15;e0119022.

doi: 10.1128/msystems.01190-22. Online ahead of print.

Natural Green Spaces, Sensitization to Allergens, and the Role of Gut Microbiota during Infancy

Vienna Buchholz[1], Sarah L Bridgman[1], Charlene C Nielsen[1], Mireia Gascon[2 3 4], Hein M Tun[5 6], Elinor Simons[7], Stuart E Turvey[8], Padmaja Subbarao[9], Tim K Takaro[10], Jeffrey R Brook[11], James A Scott[11], Piush J Mandhane[1], Anita L Kozyrskyj[1]

Affiliations expand
- PMID: 36790181

- DOI: 10.1128/msystems.01190-22

Free article

Abstract

The environment plays an instrumental role in the developmental origins of health and disease. Protective features of the environment in the development of asthma and atopy have been insufficiently studied. We used data from the CHILD (Canadian Healthy Infant Longitudinal Development) Cohort Study to examine relationships between living near natural green spaces in early infancy in Edmonton, AB, Canada and the development of atopic sensitization at 1 year and 3 years of age in a cohort of 699 infants, and whether these associations were mediated by infant gut microbiota (measured using 16s V4 amplicon sequencing) at 4 months. The Urban Planning Land Vegetation Index (uPLVI) map of the City of Edmonton was used to assess infants' exposure to natural spaces based on their home postal codes, and atopic sensitization was assessed using skin prink testing (SPTs) for common food and inhalant allergens. Our findings suggest there is a protective effect of natural green space proximity on the development of multiple inhalant atopic sensitizations at 3 years (odds ratio = 0.28 [95% CI 0.09, 0.90]). This relationship was mediated by changes to Actinobacteria diversity in infant fecal samples taken at 4 months. We also found a positive association between nature proximity and sensitization to at least one food or inhaled allergen; this association was not mediated by gut microbiota. Together, these findings underscore the importance of promoting natural urban greenspace preservation to improve child health by reducing atopic disease susceptibility. **IMPORTANCE** Our findings highlight the importance of preserving natural green space in urban settings to prevent sensitization to environmental allergens and promote early-life gut microbiota pathways to this health benefit. These findings support a mediating role of gut microbiome compositions in health and disease susceptibility. This study used unique, accurate, and comprehensive methodology to classify natural space exposure via a high-resolution topographical map of foliage subtypes within the City of Edmonton limits. These methods are improvements from other methods previously used to classify natural space exposure, such as the normalized density vegetation index from satellite imagery, which is not able to distinguish anthropogenic from green space. The use of these methods and the associations found between natural green space exposure and atopic sensitization outcomes support their use in future studies. Our findings also provide many avenues for future research including longer term follow up of this cohort and investigation of a causal role of reduced Actinobacteria diversity on atopic sensitization development.

Keywords: allergy; atopic sensitization; gut microbiome; gut microbiota; infant; infants; inhalant; microbiome; natural green space; natural space.

Rheumatology (Oxford)

. 2023 Feb 15;kead077.
doi: 10.1093/rheumatology/kead077. Online ahead of print.

Clinico-radiological correlation and prognostic value of baseline chest computed tomography in eosinophilic granulomatosis with polyangiitis

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Affiliations expand

- PMID: 36790066

- DOI: 10.1093/rheumatology/kead077

Abstract

Objectives: While chest high-resolution computed tomography (HRCT) is correlated to severity and prognosis in asthma, it has not been studied in eosinophilic granulomatosis with polyangiitis. Our objective is to study the prognostic value of baseline high-resolution computed tomography in EGPA patients.

Methods: Retrospective, multicenter observational study in three French hospitals, including EGPA patients with available chest HRCT before any systemic treatment. Two experienced radiologists blind for clinical data evaluated HRCT images using semi-quantitative scoring. HRCT characteristics were correlated with clinical features and outcome.

Results: Among 46 patients, 38 (82.6%) had abnormal parenchymal findings on HRCT, including bronchial wall thickening (69.6%), mosaic perfusion (63.0%), ground-glass opacities (32.6%), bronchiectasis (30.4%), mucous plugging (21.7%) and consolidations (17.4%). Patients were clustered into three groups depending on HRCT features: ground-

glass pattern i.e with ground-glass opacities with or without bronchial abnormalities (group 1, 28.3%), bronchial pattern (group 2, 41.3%), and extra-pulmonary pattern with no significant abnormality (group 3, 30.4%). Group 2 showed less frequent cardiac involvement (31.6 vs. 46.2 and 42.9% in groups 1 and 3), more frequent positive ANCA (52.6 vs. 0.0 and 14.3%) and higher eosinophil count (median 7,510 vs. 4,000 and 4,250/mm3). Group 1 showed worse prognosis with more frequent steroid-dependency (58.3 vs. 11.1 and 28.6%) and requirement for mepolizumab (25.0 vs. 11.1 and 7.1%). Conversely, group 2 showed a better outcome with higher rates of remission (88.9 vs. 41.6 and 71.4%).

Conclusion: Chest HRCT at diagnosis of EGPA may have prognostic value and help clinicians better manage these patients.

Keywords: Asthma; Eosinophilic granulomatosis with polyangiitis; High resolution computed tomography; Mepolizumab.

Immunotherapy
.
. 2023 Feb 15.
doi: 10.2217/imt-2022-0215. Online ahead of print.

Real-world study: drug reduction in children with allergic rhinitis and asthma receiving immunotherapy

Jorge Sánchez [1], Leidy Alvarez [2], Elizabeth García [3]
Affiliations expand

- PMID: 36789565
- DOI: 10.2217/imt-2022-0215

Abstract

Background: The reduction of pharmacological treatment after allergen immunotherapy (AIT) for house dust mites (HDMs) has been little studied in children. **Objective:** To evaluate the reduction of pharmacological treatment comparing children that receive HDM immunotherapy (AIT group) versus only pharmacotherapy. **Methods:** A historic cohort of children with rhinitis or asthma was assessed. The main outcome was the frequency of complete drug discontinuation. **Results:** 100% drug reduction was higher for rhinitis (4-year cumulative incidence: 30 vs 10.7%) and asthma (24.1 vs 10.5%) in the AIT group (n = 987) than in the pharmacotherapy group (n = 2012). **Conclusion:** Immunotherapy is associated with a significant reduction of pharmacotherapy in children. This is a marker of clinical control and could be associated with positive economic impact.

Keywords: allergen; allergy; asthma; immunotherapy; mites; pharmacotherapy; real-life; real-word; rhinitis.

Plain language summary

The benefits of allergen immunotherapy for house dust mites has been little studied in children. The usefulness of this treatment in asthma over the use of pharmacotherapy has also not been clearly evaluated. The use of immunotherapy allowed greater reductions in pharmacological treatment in children with rhinitis and asthma. Immunotherapy is a useful treatment for childhood rhinitis and asthma and reduces the risk of adverse effects from pharmacological treatments.

Acta Paediatr

. 2023 Feb 14.

doi: 10.1111/apa.16709. Online ahead of print.

Blood eosinophil levels in infants with bronchiolitis are predictive for adulthood asthma and lung function

Matti Korppi[1]
Affiliations expand

- PMID: 36789487

- DOI: 10.1111/apa.16709

No abstract available

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Multicenter Study

PLoS One

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. 2023 Feb 14;18(2):e0281742.
doi: 10.1371/journal.pone.0281742. eCollection 2023.

Health-related quality of life and its associated factors among patients with asthma: A multi-centered cross-sectional study in selected referral hospitals in Northwest Ethiopia

Eyayaw Ashete Belachew[1], Ashenafi Kibret Sendekie[1], Sumeya Tadess[1], Mekuriaw Alemayehu[2]
Affiliations expand

- PMID: 36787327
- PMCID: PMC9928093
- DOI: 10.1371/journal.pone.0281742

Free PMC article

Abstract

Background: Patients with asthma have a compromised health-related quality of life (HRQoL) due to factors related sociodemographic, clinical, and environmental factors. This study assessed the HRQoL and its determinants in patients with asthma in selected public referral hospitals in Northwest Ethiopia.

Design, setting, and participants: A multicenter facility-based cross-sectional study was conducted in selected hospitals in Northwest Ethiopia from August to October 2021. Participants were enrolled in the study using a systematic random sampling technique.

Main outcome measures: HRQoL was assessed using the asthma-specific quality of life tool Mini-Asthma Quality of Life Questionnaire (Mini-AQLQ). Simple and multivariable linear regression analyses were conducted to determine the association between independent variables and HRQoL. A p-value of < 0.05 at 95% CI was considered statistically significant.

Results: A total of 409 patients were included in the final analysis, and more than half (59.2%) of the subjects had a good health-related quality of life. Regarding HRQoL determinants, asthma control score (β = 0.14, 95% CI: 0.09, 0.17; p 0.001), insurance user (β = 0.15, 95% CI: 0.01, 0.29); p = 0.042), the high role of patient enablement (β = 0.39, 95% CI: 0.25, 0.54; p 0.001), belief in asthma medication (β = -0.23, 95% CI: -0.36, -0.10;p = 0.001), non-adherence to guidelines (β = -0.30, 95% CI: -0.47, -0.15; p < 0.001), and being homemaker (β = -0.21, 95% CI: -0.39, -0.01; p = 0.040) were the significant predictors of HRQoL.

Conclusion: Overall, more than half of the study participants were found to have good HRQoL. HRQoL among adults with asthma was largely dependent on the level of asthma control. Socio-demographic, clinical, healthcare-related, and medication-related variables were significantly associated with health-related quality of life. Therefore, healthcare providers should include comprehensive asthma education along with an integrated treatment plan to improve asthma control and the HRQoL of patients.

Conflict of interest statement

The authors declared That they have no Competing interest.

- 52 references
- 3 figures

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JAMA

. 2023 Feb 14;329(6):490-501.
doi: 10.1001/jama.2023.0128.

Discriminative Accuracy of the CAPTURE Tool for Identifying Chronic Obstructive Pulmonary Disease in US Primary Care Settings

Fernando J Martinez[1], MeiLan K Han[2], Camden Lopez[3], Susan Murray[3], David Mannino[4], Stacey Anderson[3], Randall Brown[3], Rowena Dolor[5], Nancy Elder[6], Min Joo[7], Irfan Khan[8], Lyndee M Knox[9], Catherine Meldrum[2], Elizabeth Peters[1], Cathie Spino[3], Hazel Tapp[10], Byron Thomashow[11], Linda Zittleman[12], Barry Make[13], Barbara P Yawn[14]; CAPTURE Study Group
Collaborators, Affiliations expand

- PMID: 36786790
- PMCID: PMC9929696 (available on 2023-08-14)
- DOI: 10.1001/jama.2023.0128

Abstract

Importance: Chronic obstructive pulmonary disease (COPD) is underdiagnosed in primary care.

Objective: To evaluate the operating characteristics of the CAPTURE (COPD Assessment in Primary Care To Identify Undiagnosed Respiratory Disease and Exacerbation Risk) screening tool for identifying US primary care patients with undiagnosed, clinically significant COPD.

Design, setting, and participants: In this cross-sectional study, 4679 primary care patients aged 45 years to 80 years without a prior COPD diagnosis were enrolled by 7 primary care practice-based research networks across the US between October 12, 2018, and April 1, 2022. The CAPTURE questionnaire responses, peak expiratory flow rate, COPD Assessment Test scores, history of acute respiratory illnesses, demographics, and spirometry results were collected.

Exposure: Undiagnosed COPD.

Main outcomes and measures: The primary outcome was the CAPTURE tool's sensitivity and specificity for identifying patients with undiagnosed, clinically significant COPD. The secondary outcomes included the analyses of varying thresholds for defining a positive screening result for clinically significant COPD. A positive screening result was defined as (1) a CAPTURE questionnaire score of 5 or 6 or (2) a questionnaire score of 2, 3, or 4 together with a peak expiratory flow rate of less than 250 L/min for females or less than 350 L/min for males. Clinically significant COPD was defined as spirometry-defined COPD (postbronchodilator ratio of forced expiratory volume in the first second of expiration [FEV1] to forced vital capacity [FEV1:FVC] <0.70 or prebronchodilator FEV1:FVC <0.65 if postbronchodilator spirometry was not completed) combined with either an FEV1 less than 60% of the predicted value or a self-reported history of an acute respiratory illness within the past 12 months.

Results: Of the 4325 patients who had adequate data for analysis (63.0% were women; the mean age was 61.6 years [SD, 9.1 years]), 44.6% had ever smoked cigarettes, 18.3% reported a prior asthma diagnosis or use of inhaled respiratory medications, 13.2% currently smoked cigarettes, and 10.0% reported at least 1 cardiovascular comorbidity. Among the 110 patients (2.5% of 4325) with undiagnosed, clinically significant COPD, 53 had a positive screening result with a sensitivity of 48.2% (95% CI, 38.6%-57.9%) and a specificity of 88.6% (95% CI, 87.6%-89.6%). The area under the receiver operating curve for varying positive screening thresholds was 0.81 (95% CI, 0.77-0.85).

Conclusions and relevance: Within this US primary care population, the CAPTURE screening tool had a low sensitivity but a high specificity for identifying clinically significant COPD defined by presence of airflow obstruction that is of moderate severity or accompanied by a history of acute respiratory illness. Further research is needed to optimize performance of the screening tool and to understand whether its use affects clinical outcomes.

Conflict of interest statement

Conflict of Interest Disclosures: Dr Martinez reported receiving grants from Chiesi Farmaceutici, CSL Behring, GSK (formerly GlaxoSmithKline), Medtronic, Novartis, Polarean, Sanofi, and Regeneron; receiving personal fees from AstraZeneca, Boehringer Ingelheim, GSK, Polarean, Pulmatrix, Sanofi, Regeneron, Theravance Biopharma, and Viatris; receiving travel reimbursement from AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, CSL Behring, and GSK; and having a patent for the CAPTURE screening tool that is licensed to Weill Cornell Medicine. Dr Han reported receiving personal fees from GSK, AstraZeneca, Verona Pharma, Merck, MDBriefCase, Mylan (now part of Viatris), DevPro Biopharma, Aerogen, Polarean, Regeneron, UpToDate, Altesa BioSciences, Medscape, Integrity, Boehringer Ingelheim, Cipla, Chiesi Farmaceutici, Novartis, Pulmonx, Teva Pharmaceuticals, and the National Association for Continuing Education; receiving grants from the American Lung Association, AstraZeneca, Boehringer Ingelheim, the COPD Foundation, Biodesix, Gala Therapeutics, Medtronic, Sanofi, Sunovion, and Nuvaira Inc; and having stock options in Altesa BioSciences and Meissa Vaccines. Dr Mannino reported receiving personal fees from GSK, AstraZeneca, UpToDate, and Schlesinger law firm. Dr Brown reported receiving personal fees from Teva Pharmaceuticals. Dr Khan reported being the CEO and receiving standard clinical trial site and enrollment fees for study execution paid to Circuit Clinical (employer and clinical trials company). Dr Spino reported receiving grants from the Three Lakes Foundation. Dr Thomashow reported receiving personal fees from GSK, Boehringer Ingelheim, and Reckitt Health and being the co-founder and chief medical officer (volunteer position) of the COPD Foundation, which is a nonprofit organization. Dr Make reported receiving grants from the American Lung Association and the US Department of Defense; receiving personal fees from the American College of Chest Physicians, AstraZeneca, GSK, Integritas, Boehringer Ingelheim, Mylan, Novartis, Optimum Patient Care Global, Projects in Knowledge, IQVIA (formerly Quintiles and IMS Health), Third Pole, University of Wisconsin, WebMD, and Mt Sinai; and having a patent and receiving royalties from Wolters Kluwer Health (UpToDate). Dr Yawn reported receiving personal fees from GSK, Teva Pharmaceuticals, AstraZeneca, and Boehringer Ingelheim. No other disclosures were reported.

Comment in

- doi: 10.1001/jama.2021.23255

supplementary info

Publication types, MeSH terms, Grant supportexpand

full text links

. 2023 Feb 13;94(1):e2023028.
doi: 10.23750/abm.v94i1.13474.

Effects of benralizumab in a population of patients affected by severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: a real life study

Carla Santomasi[1], Enrico Buonamico[2], Silvano Dragonieri[3], Lucia Iannuzzi[4], Andrea Portacci[5], Nicola Quaranta[6], Giovanna Elisiana Carpagnano[7]
Affiliations expand

- PMID: 36786266

- DOI: 10.23750/abm.v94i1.13474

Free article

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a frequent comorbidity in severe eosinophilic asthma (SEA), which may contribute to the loss of asthma control. CRSwNP and SEA share a T2-mediated mechanism and the use of some anti-asthma monoclonal antibodies has recently been extended to CRSwNP. Unlike dupilumab and omalizumab, benralizumab approval for CRSwNP is ongoing. We aimed to evaluate the efficacy of benralizumab efficacy on SEA and on CRSwNP in patients affected by both pathologies in a real life setting.

Methods: 17 patients affected by both SEA and CRSwNP participated to our study. At baseline (T0) and at one year after benralizumab initiation (T1), all participants underwent spirometry, exhaled nitric oxide (FeNO), Asthma Control Test (ACT), nasal endoscopy with Nasal Polyp Score (NPS), nasal cytology and Sino-Nasal Outcome Test 22 (SNOT 22).The continuous oral corticosteroid therapy (OCS), the number of year exacerbations and the need for sinus surgery were also evaluated for each patient.

Results: At T1, a marked reduction of SNOT-22, NPS, nasal eosinophils and neutrophils count were shown compared to T0. Moreover, at T1 ACT was significantly increased and FeNO, exacerbations/year and mean OCS dosage were significantly reduced compared to T0.

Conclusions: Our real-life study demonstrates the efficacy of benralizumab not only on SEA but also on nasal cytology and on nasal polyposis, confirming that patients affected by

both SEA and CRSwNP may receive a considerable benefit from anti-IL5 receptor, treating both the comorbidities at once.

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Review

Eur J Immunol

. 2023 Feb 13;e2250106.

doi: 10.1002/eji.202250106. Online ahead of print.

Lung epithelial cells: upstream targets in type 2-high asthma

Sahine Lameire[1,2], Hamida Hammad[1,2]

Affiliations expand

- PMID: 36781404

- DOI: 10.1002/eji.202250106

Abstract

Over the last years, technological advances in the field of asthma have led to the identification of two disease endotypes, namely type 2-high and type 2-low asthma, characterized by different pathophysiologic mechanisms at a cellular and molecular level. Although specific immune cells are important contributors to each of the recognized asthma endotype, the lung epithelium is now regarded as a crucial player able to orchestrate responses to inhaled environmental triggers such as allergens and microbes. The impact of the epithelium goes beyond its physical barrier. It is nowadays considered as a part of the innate immune system that can actively respond to insults. Activated epithelial cells, by producing a specific set of cytokines, trigger innate and adaptive immune cells to cause pathology. Here, we review how the epithelium contributes to the development of

Th2 sensitization to allergens and asthma with a "type 2-high" signature, in both murine models and human studies of this asthma endotype. We also discuss epithelial responses to respiratory viruses, like RV, RSV and SARS-CoV-2, and how these triggers influence not only asthma development but also asthma exacerbation. Finally, we also summarize the results of promising clinical trials using biologicals targeting epithelial-derived cytokines in asthmatic patients.

Keywords: Asthma; Epithelial cells; Microbiome; SARS-CoV-2; Th2.

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19
Int J Immunogenet

. 2023 Feb 13.
doi: 10.1111/iji.12615. Online ahead of print.

Interleukin 17A and 17F polymorphisms and asthma susceptibility: Correspondence

Amnuay Kleebayoon[1], Viroj Wiwanitkit[2]
Affiliations expand

- PMID: 36779706
- DOI: 10.1111/iji.12615

No abstract available

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20
Int J Immunogenet
.
. 2023 Feb 13.
doi: 10.1111/iji.12616. Online ahead of print.

IL-17A and IL-17F polymorphisms and asthma risk: A meta-analysis

Young Ho Lee[1]
Affiliations expand

- PMID: 36779703
- DOI: 10.1111/iji.12616

No abstract available

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21
J Asthma
.
. 2023 Feb 15;1-10.
doi: 10.1080/02770903.2023.2176775. Online ahead of print.

Scoping review: multiple stakeholders and child asthma management interventions

Samuel Adabla[1], Laura A Nabors[1], Olutosin Sanyaolu[1], Afolakemi Olaniyan[1], Jonathan A Bernstein[2]
Affiliations expand

- PMID: 36744817

- DOI: 10.1080/02770903.2023.2176775

Abstract

Objective: This study reviewed research to identify interventions aimed at improving asthma management among children by educating parents and other professionals.

Data sources: PubMed, Medline, and Embase databases were utilized.

Study selections: Three databases were searched for child asthma management interventions published between 2012-2022 in English. Search terms included children, asthma, intervention(s), community pediatrics, coaches, schools, and stakeholders. Inclusion criteria were being an experimental study focused on children with asthma (birth-18 years), including stakeholder involvement, education, and a community focus. The search yielded 153 articles; nine were reviewed.

Results: In general, stakeholders developed programs that resulted in improvements in asthma symptoms, knowledge of asthma management, perceptions of health care, and decreased emergency health care visits. Successful interventions involved education about asthma management, providing medications, and partnerships with school staff, healthcare teams, and community members. Effective coordination and communication contributed to successful program implementation. Using technology for asthma management education was effective in tracking access to care and facilitated the delivery of medications.

Conclusion: The findings indicate that interventions were effective in improving child asthma management. Stakeholder partnerships were critical to the effectiveness of interventions. Marketing the intervention and encouraging communication with parents also fostered success. Being able to assess the home environment and staying in contact with parents were barriers to these interventions. Conducting randomized controlled trials using the interventions found effective in these studies to assess change in symptoms and emergency care visits over time would yield important information about their long-term success and cost for implementation.

Keywords: Asthma; asthma management; children; stakeholder involvement.

Life Sci
.
. 2023 Feb 15;315:121373.
doi: 10.1016/j.lfs.2023.121373. Epub 2023 Jan 5.

Corticosteroid treatment attenuates anxiety and mPFC-amygdala circuit dysfunction in allergic asthma

Kolsoum Dehdar[1], Morteza Mooziri[2], Ali Samii Moghaddam[2], Morteza Salimi[3], Milad Nazari[4], Samaneh Dehghan[5], Hamidreza Jamaati[1], Alireza Salimi[1], Mohammad Reza Raoufy[6]
Affiliations expand
- PMID: 36621536

- DOI: 10.1016/j.lfs.2023.121373

Abstract

Aims: Allergic asthma is associated with anxiety-related behaviors, leading to poor quality of life. Previous studies mainly described the neuropathophysiology of asthma-induced anxiety. However, the effects of corticosteroids, the most common anti-inflammatory agents for asthma treatment, on the neurophysiological foundations of allergic asthma-induced anxiety are unexplored.

Main methods: Here, we evaluated lung and brain inflammation as well as anxiety in an animal model of allergic asthma pretreated with inhaled fluticasone propionate. Furthermore, to define the neurophysiological bases of these conditions, we studied the medial prefrontal cortex (mPFC)-amygdala circuit, which is previously shown to accompany asthma-induced anxiety.

Key findings: Our data showed that allergen induces anxiety, mPFC and amygdala inflammation, as well as disruptions in the local and long-range oscillatory activities within the mPFC-amygdala circuit. Interestingly, we observed a roughly consistent trend of

changes with inhaled fluticasone pretreatment. Namely, the asthma-induced behavioral, inflammatory, and neurophysiological changes were partly, but not totally, prevented by inhaled fluticasone pretreatment.

Significance: We suggest that early treatment of asthmatic patients with inhaled corticosteroids improves mPFC-amygdala circuit function by attenuating neuroinflammation leading to reduced anxiety. These findings could lead clinical guidelines of asthma to consider the neuropsychiatric disorders of patients in treatment recommendations.

Keywords: Amygdala; Anxiety; Asthma; Corticosteroid; mPFC.

Conflict of interest statement

Declaration of competing interest The authors declare that there are no conflicts of interest.

supplementary info

MeSH terms, Substancesexpand

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Editorial

Am J Respir Crit Care Med

. 2023 Feb 15;207(4):375-376.

doi: 10.1164/rccm.202212-2302ED.

Asthma: Closing in on the Biology of a Complex Life-course Disease

Andrew Bush[1 2], Fernando Holguin[3], Celeste Porsbjerg[4], Sejal Saglani[5]

Affiliations expand

- PMID: 36598866

- DOI: 10.1164/rccm.202212-2302ED

No abstract available

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Environ Res

. 2023 Feb 15;219:115180.

doi: 10.1016/j.envres.2022.115180. Epub 2022 Dec 28.

Are air quality perception and $PM_{2.5}$ exposure differently associated with cardiovascular and respiratory disease mortality in Brussels? Findings from a census-based study

Terhi Kangas[1], Sylvie Gadeyne[2], Wouter Lefebvre[3], Charlotte Vanpoucke[4], Lucía Rodriguez-Loureiro[2]

Affiliations expand

- PMID: 36584842

- DOI: 10.1016/j.envres.2022.115180

Abstract

Background: There is ample evidence that air pollution increases mortality risk, but most studies are based on modelled estimates of air pollution, while the subjective perception of air quality is scarcely assessed. We aimed to compare the effects of objective and subjective exposure to air pollution on cardiorespiratory mortality in Brussels, Belgium.

Methods: Data consisted of the 2001 Belgian census linked to registry-based mortality data for the follow-up period 2001-2014. We included individuals aged >30 years of age residing in Brussels at baseline (2001). Air pollution exposure was assessed with objective

(modelled annual mean concentrations of $PM_{2.5}$ in micrograms per cubic metre, µg/m^3) and subjective indicators (poor self-reported air quality perception in the census). We used Cox Proportional Hazard models with age as the underlying time scale to evaluate associations with cardiovascular disease (CVD) and respiratory disease mortality, and separately, ischaemic heart disease (IHD), cerebrovascular disease, and COPD excluding asthma mortality. We specified single- and two-exposure models and evaluated effect modification by neighbourhood unemployment rate.

Results: 437,340 individuals were included at baseline. During follow-up (2001-2014), 22,821 (5%) individuals had died from CVDs and 8572 (2%) from respiratory diseases. In single-exposure models, $PM_{2.5}$ was significantly associated with an increased risk in CVD and IHD mortality (e.g. for IHD, per 5 µg/m^3 increase: Hazard Ratio, HR:1.22, 95%CI:1.08-1.37), and poor air quality perception with COPD excluding asthma mortality (HR:1.23, 95%CI:1.15-1.33). Associations remained significant in the two-exposure models, and additionally, perception was associated with respiratory disease mortality. Associations became gradually stronger with increasing neighbourhood unemployment rate [e.g. in the highest, Q3: $PM_{2.5}$ and cerebrovascular disease mortality (HR:1.53, 95%CI:1.04-2.24)].

Conclusion: Our findings suggest that objective and subjective exposure to air pollution increased the risk of dying from cardiovascular and respiratory diseases respectively in Brussels. These results encourage policies reducing pollution load in Brussels whilst considering socio-economic inequalities.

Keywords: Air quality perception; Ambient air pollution; Cardiovascular disease; Mortality; Particulate matter; Respiratory disease.

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:Dr. Prof. Sylvie Gadeyne reports financial support was provided by Brussels Institute for scientific research.

. 2023 Feb 15;219:115102.
doi: 10.1016/j.envres.2022.115102. Epub 2022 Dec 21.

Exposure to ambient ultrafine particles and allergic sensitization in children up to 16 years

Femke Bouma[1], Gerard Hoek[2], Gerard H Koppelman[3], Judith M Vonk[4], Jules Kerckhoffs[2], Roel Vermeulen[5], Ulrike Gehring[2]
Affiliations expand

- PMID: 36565840

- DOI: 10.1016/j.envres.2022.115102

Free article

Abstract

Background: Few epidemiological studies so far have investigated the role of long-term exposure to ultrafine particles (UFP) in inhalant and food allergy development.

Objectives: The purpose of this study was to assess the association between UFP exposure and allergic sensitization to inhalant and food allergens in children up to 16 years old in the Netherlands.

Methods: 2295 participants of a prospective birth cohort with IgE measurements to common inhalant and food allergens at ages 4, 8, 12 and/or 16 were included in the study. Annual average UFP concentrations were estimated for the home addresses at birth and at the time of the IgE measurements using land-use regression models. Generalized estimating equations were used for the assessment of overall and age-specific associations between UFP exposure and allergic sensitization. Additionally, single- and two-pollutant models with NO_2, $PM_{2.5}$, $PM_{2.5}$ absorbance and PM_{10} were assessed.

Results: We found no significant associations between UFP exposure and allergic sensitization to inhalant and food allergens (OR (95% CI) ranging from 1.02 (0.95-1.10) to 1.05 (0.98-1.12), per IQR increment). NO_2, $PM_{2.5}$, $PM_{2.5}$ absorbance and PM_{10} showed significant associations with sensitization to food allergens (OR (95% CI) ranging from 1.09 (1.00-1.20) to 1.23 (1.06-1.43) per IQR increment). NO_2, $PM_{2.5}$, $PM_{2.5}$ absorbance and PM_{10} were not associated with sensitization to inhalant allergens. For NO_2, $PM_{2.5}$ and $PM_{2.5}$ absorbance, the associations with sensitization to food allergens persisted in two-pollutant models with UFP.

Conclusion: This study found no association between annual average exposure to UFP and allergic sensitization in children up to 16 years of age. NO_2, $PM_{2.5}$, $PM_{2.5}$ absorbance and PM_{10} were associated with sensitization to food allergens.

Keywords: Air pollution; Allergy; Children; IgE sensitization; Inhalant and food allergens; Ultrafine particles.

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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Editorial

Am J Respir Crit Care Med

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. 2023 Feb 15;207(4):377-379.
doi: 10.1164/rccm.202212-2297ED.

Over-the-counter Dispensing: Widening Access to Inhaled Corticosteroid/Formoterol Reliever Therapy

Richard Beasley[1], Lee Hatter[1]

Affiliations expand

- PMID: 36548806

- DOI: 10.1164/rccm.202212-2297ED

No abstract available

Comment on

- A Call for the United States to Accelerate the Implementation of Reliever Combination Inhaled Corticosteroid-Formoterol Inhalers in Asthma.
  Krings JG, Gerald JK, Blake KV, Krishnan JA, Reddel HK, Bacharier LB, Dixon AE, Sumino K, Gerald LB, Brownson RC, Persell SD, Clemens CJ, Hiller KM, Castro M, Martinez FD.Am J Respir Crit Care Med. 2023 Feb 15;207(4):390-405. doi: 10.1164/rccm.202209-1729PP.PMID: 36538711 No abstract available.

supplementary info

Publication types, MeSH terms, Substancesexpand

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Am J Respir Crit Care Med

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. 2023 Feb 15;207(4):390-405.
doi: 10.1164/rccm.202209-1729PP.

A Call for the United States to Accelerate the Implementation of Reliever Combination Inhaled Corticosteroid-Formoterol Inhalers in Asthma

James G Krings[1], Joe K Gerald[2,3], Kathryn V Blake[4], Jerry A Krishnan[5], Helen K Reddel[6], Leonard B Bacharier[7], Anne E Dixon[8], Kaharu Sumino[1], Lynn B Gerald[9], Ross C Brownson[10,11], Stephen D Persell[12,13], Conrad J Clemens[14], Katherine M Hiller[15], Mario Castro[16], Fernando D Martinez[3]

Affiliations expand

- PMID: 36538711

- DOI: 10.1164/rccm.202209-1729PP

No abstract available

Comment in

- Over-the-counter Dispensing: Widening Access to Inhaled Corticosteroid/Formoterol Reliever Therapy.
  Beasley R, Hatter L.Am J Respir Crit Care Med. 2023 Feb 15;207(4):377-379. doi: 10.1164/rccm.202212-2297ED.PMID: 36548806 No abstract available.

supplementary info

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Editorial

Am J Respir Crit Care Med

. 2023 Feb 15;207(4):386-388.
doi: 10.1164/rccm.202212-2231ED.

A Few Bad Airways Can Wreak Havoc: Recognizing Asthma as a Local Disorder

Kenneth Lutchen [1]

Affiliations expand

- PMID: 36516460
- DOI: 10.1164/rccm.202212-2231ED

No abstract available

Comment on

- Heterogeneity of Airway Smooth Muscle Remodeling in Asthma.
  James AL, Donovan GM, Green FHY, Mauad T, Abramson MJ, Cairncross A, Noble PB, Elliot JG.Am J Respir Crit Care Med. 2023 Feb 15;207(4):452-460. doi: 10.1164/rccm.202111-2634OC.PMID: 36399661

supplementary info

Review

Ann Work Expo Health

. 2023 Feb 13;67(2):163-181.
doi: 10.1093/annweh/wxac074.

The Relationship Between Potential Occupational Sensitizing Exposures and Asthma: An Overview of Systematic Reviews

Annett Dalbøge[1,2], Henrik Albert Kolstad[1], Charlotte Suppli Ulrik[3], David Lee Sherson[4,5], Harald William Meyer[6], Niels Ebbehøj[6], Torben Sigsgaard[7], Jan-Paul Zock[8], Xaver Baur[9], Vivi Schlünssen[10,7]
Affiliations expand

- PMID: 36472234

- DOI: 10.1093/annweh/wxac074

Abstract

Objectives: The aim was to identify, appraise, and synthesize the scientific evidence of the relationship between potential occupational sensitizing exposures and the development of asthma based on systematic reviews.

Methods: The study was conducted as an overview of systematic reviews. A systematic literature search was conducted for systematic reviews published up to 9 February 2020. Eligibility study criteria included persons in or above the working age, potential occupational sensitizing exposures, and outcomes defined as asthma. Potential occupational sensitizing exposures were divided into 23 main groups comprising both

subgroups and specific exposures. Two reviewers independently selected studies, extracted study data, assessed study quality, and evaluated confidence in study results and level of evidence of the relationship between potential occupational sensitizing exposures and asthma.

Results: Twenty-seven systematic reviews were included covering 1242 studies and 486 potential occupational sensitizing exposures. Overall confidence in study results was rated high in three systematic reviews, moderate in seven reviews, and low in 17 reviews. Strong evidence for the main group of wood dusts and moderate evidence for main groups of mites and fish was found. For subgroups/specific exposures, strong evidence was found for toluene diisocyanates, Aspergillus, Cladosporium, Penicillium, and work tasks involving exposure to laboratory animals, whereas moderate evidence was found for 52 subgroups/specific exposures.

Conclusions: This overview identified hundreds of potential occupational sensitizing exposures suspected to cause asthma and evaluated the level of evidence for each exposure. Strong evidence was found for wood dust in general and for toluene diisocyanates, Aspergillus, Cladosporium, Penicillium, and work tasks involving exposure to laboratory animals.

Keywords: Allergen; allergy; lung disease; respiratory symptom; work.

J Affect Disord

. 2023 Feb 15;323:21-29.
doi: 10.1016/j.jad.2022.11.045. Epub 2022 Nov 22.

Multi-dimensional analyses of the associations between depression, nocturnal awakening and asthmatic outcomes

Zhigang Hu [1], Yufeng Tian [2], Xinyu Song [3], Ke Hu [4], Ailan Yang [5]
Affiliations expand

- PMID: 36427647

- DOI: 10.1016/j.jad.2022.11.045

Abstract

Background: Depression plays an important role in the occurrence and development of asthma. Nocturnal awakening secondary to asthma is a crucial sign of the deterioration of asthmatic outcomes. This study plans to determine the associations between depression, nocturnal awakening and asthmatic outcomes by using multi-dimensional analyses.

Methods: Study population came from the Adult Asthma Call-Back Survey 2013-2017. Multivariable regression analysis with binomial or Poisson models, dose-dependent analysis and mediation analysis were used to explore the associations between depression and nocturnal awakening with asthmatic episodes/attacks, emergency room (ER) and hospital visits.

Results: 18,684 physician-diagnosis asthmatics were included into this study. This population consisted of 31.4 % with nocturnal awakening and 37.6 % with depression. Multivariable binomial analyses suggested that nocturnal awakening and depression were positively associated with asthmatic episodes/attacks and ER visits. Dose-dependent analyses demonstrated that the increase of nocturnal awakening was positively associated with the increase of depression and three asthmatic outcomes. Asthmatics with depression had the higher prevalence (adjusted OR = 1.17, 95%CI: 1.08-1.27) and frequency (adjusted RR = 1.08, 95%CI: 1.07-1.10) of nocturnal awakening than those without depression. Mediation analyses suggested that clarification of verbiage denoted trivial effect of depression on the associations between nocturnal awakening with asthmatic outcomes, while nocturnal awakening mildly mediated these associations between depression with asthmatic episodes/attacks (15.26 %, 95%CI: 7.29 %-28.7 %) and ER visits (13.29 %, 95%CI: 5.33 %-44.12 %).

Limitation: The cross-sectional nature limited inferences on causality.

Conclusions: Our findings showed that depression and nocturnal awakening might affect asthmatic outcomes. Nocturnal awakening harbored the mediated effect in the correlations between depression and asthmatic outcomes.

Keywords: Asthma; Depression; Dose-dependent; Mediation analysis; Nocturnal awakening.

Conflict of interest statement

Conflict of interest The authors declare that they have no conflict of interest.

Editorial

Am J Respir Crit Care Med

. 2023 Feb 15;207(4):383-385.
doi: 10.1164/rccm.202211-2074ED.

The Intersection between Autoimmunity, Macrophage Dysfunction, Endotype, and Exacerbations in Severe Asthma

Ryan C Murphy[1,2], Eric D Morrell[3], Teal S Hallstrand[1,2]
Affiliations expand

- PMID: 36413362

- DOI: 10.1164/rccm.202211-2074ED

No abstract available

Comment on

- Autoantibody-mediated Macrophage Dysfunction in Patients with Severe Asthma with Airway Infections.
  Son K, Miyasaki K, Salter B, Loukov D, Chon J, Zhao N, Radford K, Huang C, LaVigne N, Dvorkin-Gheva A, Lacy P, Ho T, Bowdish DME, Nair P, Mukherjee M.Am J Respir Crit Care Med. 2023 Feb 15;207(4):427-437. doi: 10.1164/rccm.202206-1183OC.PMID: 36287613

Am J Respir Crit Care Med
.
. 2023 Feb 15;207(4):406-415.
doi: 10.1164/rccm.202203-0444OC.

Plasticity of Individual Lung Function States from Childhood to Adulthood

Gang Wang[1,2,3,4], Jenny Hallberg[2,5], Rosa Faner[6,7], Hans-Jacob Koefoed[8], Simon Kebede Merid[2], Susanna Klevebro[2,5], Sophia Björkander[2], Olena Gruzieva[3,9], Göran Pershagen[3,9], Marianne van Hage[10], Stefano Guerra[11,12], Matteo Bottai[13], Antonios Georgelis[9], Ulrike Gehring[14], Anna Bergström[3,9], Judith M Vonk[8,15], Inger Kull[2,5], Gerard H Koppelman[8,16], Alvar Agusti[6,7,17,18], Erik Melén[2,5]
Affiliations expand

- PMID: 36409973

- DOI: 10.1164/rccm.202203-0444OC

Abstract

Rationale: Recent evidence highlights the importance of optimal lung development during childhood for health throughout life. **Objectives:** To explore the plasticity of individual lung function states during childhood. **Methods:** Prebronchodilator FEV_1 *z*-scores determined at age 8, 16, and 24 years in the Swedish population-based birth cohort BAMSE (Swedish abbreviation for Child [Barn], Allergy, Milieu, Stockholm, Epidemiological study) (*N* = 3,069) were used. An unbiased, data-driven dependent mixture model was applied to explore lung function states and individual state chains. Lung function catch-up was defined as participants moving from low or very low states to normal or high or very high states, and growth failure as moving from normal or high or very high states to low or very low states. At 24 years, we compared respiratory symptoms, small airway function (multiple-breath washout), and circulating inflammatory protein levels, by using proteomics, across states. Models were replicated in the independent Dutch population-based PIAMA (Prevention and Incidence of Asthma and Mite Allergy) cohort. **Measurements and Main Results:** Five lung function states were identified in BAMSE. Lung function catch-up and growth failure were observed in 74 (14.5%) BAMSE

participants with low or very low states and 36 (2.4%) participants with normal or high or very high states, respectively. The occurrence of catch-up and growth failure was replicated in PIAMA. Early-life risk factors were cumulatively associated with the very low state, as well as with catch-up (inverse association) and growth failure. The very low state as well as growth failure were associated with respiratory symptoms, airflow limitation, and small airway dysfunction at adulthood. Proteomics identified IL-6 and CXCL10 (C-X-C motif chemokine 10) as potential biomarkers of impaired lung function development. **Conclusions:** Individual lung function states during childhood are plastic, including catch-up and growth failure.

Keywords: asthma; early life risk factors; inflammation; multiple-breath washout; respiratory health.

Comment in

- Evolution of Lung Function within Individuals: Clinical Insights and Data-driven Methods.
  Custovic A, Fontanella S.Am J Respir Crit Care Med. 2023 Feb 15;207(4):379-381. doi: 10.1164/rccm.202212-2226ED.PMID: 36515972 No abstract available.

Am J Respir Crit Care Med

. 2023 Feb 15;207(4):452-460.
doi: 10.1164/rccm.202111-2634OC.

Heterogeneity of Airway Smooth Muscle Remodeling in Asthma

Alan L James[1,2], Graham M Donovan[3], Francis H Y Green[4], Thais Mauad[5], Michael J Abramson[6], Alvenia Cairncross[7], Peter B Noble[7], John G Elliot[1,7]
Affiliations expand

- PMID: 36399661

- DOI: 10.1164/rccm.202111-2634OC

Abstract

Rationale: Ventilatory defects in asthma are heterogeneous and may represent the distribution of airway smooth muscle (ASM) remodeling. **Objectives:** To determine the distribution of ASM remodeling in mild-severe asthma. **Methods:** The ASM area was measured in nine airway levels in three bronchial pathways in cases of nonfatal (n = 30) and fatal asthma (n = 20) and compared with control cases without asthma (n = 30). Correlations of ASM area within and between bronchial pathways were calculated. Asthma cases with 12 large and 12 small airways available (n = 42) were classified on the basis of the presence or absence of ASM remodeling (more than two SD of mean ASM area of control cases, n = 86) in the large or small airway or both. **Measurements and Main Results:** ASM remodeling varied widely within and between cases of nonfatal asthma and was more widespread and confluent and more marked in fatal cases. There were weak correlations of ASM between levels within the same or separate bronchial pathways; however, predictable patterns of remodeling were not observed. Using mean data, 44% of all asthma cases were classified as having no ASM remodeling in either the large or small airway despite a three- to 10-fold increase in the number of airways with ASM remodeling and 81% of asthma cases having ASM remodeling in at least one large and small airway. **Conclusions:** ASM remodeling is related to asthma severity but is heterogeneous within and between individuals and may contribute to the heterogeneous functional defects observed in asthma. These findings support the need for patient-specific targeting of ASM remodeling.

Comment in

- A Few Bad Airways Can Wreak Havoc: Recognizing Asthma as a Local Disorder. Lutchen K.Am J Respir Crit Care Med. 2023 Feb 15;207(4):386-388. doi: 10.1164/rccm.202212-2231ED.PMID: 36516460 No abstract available.

supplementary info

MeSH terms, Grant supportexpand

full text links

Randomized Controlled Trial

. 2023 Feb 15;207(4):487-490.
doi: 10.1164/rccm.202206-1132LE.

A Pilot Randomized Controlled Trial of an Intervention to Improve Perception of Lung Function in Older Adults with Asthma

Jonathan M Feldman[1,2], Jyoti Ankam[3], Michele Barry[3], Natalie Fruchter[1], Jacqueline Becker[3], Sunit Jariwala[4], Chang Shim[5,6], Juan P Wisnivesky[3], Alex D Federman[3]
Affiliations expand

- PMID: 36343280

- DOI: 10.1164/rccm.202206-1132LE

No abstract available

supplementary info

Publication types, MeSH terms, Substances, Grant supportexpand

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Am J Respir Crit Care Med

. 2023 Feb 15;207(4):427-437.
doi: 10.1164/rccm.202206-1183OC.

Autoantibody-mediated Macrophage Dysfunction in Patients with Severe Asthma with Airway Infections

Kiho Son[1,2], Kate Miyasaki[1,2], Brittany Salter[1], Dessi Loukov[1,3], Joseph Chon[1,3], Nan Zhao[1], Katherine Radford[1,2], Chynna Huang[1,2], Nicola LaVigne[1,2], Anna Dvorkin-

Gheva[1,3], Paige Lacy[4], Terence Ho[1,2], Dawn M E Bowdish[1,2,3], Parameswaran Nair[1,2], Manali Mukherjee[1,2,3]
Affiliations expand

- PMID: 36287613

- DOI: 10.1164/rccm.202206-1183OC

Abstract

Rationale: Localized autoimmune responses have been reported in patients with severe eosinophilic asthma, characterized by eosinophil degranulation and airway infections. **Objective:** To determine the presence of autoantibodies against macrophage scavenger receptors within the airways and their effects on macrophage function and susceptibility to infection. **Methods:** Anti-EPX (eosinophil peroxidase), anti-MARCO (macrophage receptor with collagenous structure) IgG titers, and T1 and T2 (type 1/2) cytokines were measured in 221 sputa from 143 well-characterized patients with severe asthma. Peripheral monocytes and MDMs (monocyte-derived macrophages) isolated from healthy control subjects were treated with immunoprecipitated immunoglobulins from sputa with high anti-MARCO titers or nonspecific IgG to assess uptake of *Streptococcus pneumoniae* or response to the bacterial product LPS. **Measurements and Main Results:** Anti-MARCO IgG was detected in 36% of patients, with significantly higher titers (up to 1:16) in patients with mixed granulocytic sputa, indicative of airway infections. Multivariate regression analysis confirmed increased frequency of degranulation (free eosinophil granules), increased blood eosinophils (indicative of high T2 burden), increased sputum total cell count, peripheral blood leukocytes (indicative of infection), and lymphopenia were associated with increased anti-MARCO IgG titers; IL-15 (odds ratio [OR], 1.79; confidence interval [CI], 1.19-2.70), IL-13 (OR, 1.06; CI, 1.02-1.12), and IL-12p70 (OR, 3.34; CI, 1.32-8.40) were the associated cytokines. Patients with anti-MARCO antibodies had higher chances of subsequent infective versus eosinophilic exacerbations (P = 0.01). MDMs treated with immunoprecipitated immunoglobulins (anti-MARCO$^+$ sputa) had reduced bacterial uptake by 39% ± 15% and significantly reduced release of IL-10 and granulocyte-macrophage colony-stimulating factor (GM-CSF) (P < 0.05) in response to an LPS stimulus. **Conclusions:** Autoantibodies against macrophage scavenger receptors in eosinophilic asthma airways may impede effective host defenses and lead to recurrent infective bronchitis.

Keywords: MARCO; autoantibodies; infections; macrophage; severe asthma.

Comment in

- The Intersection between Autoimmunity, Macrophage Dysfunction, Endotype, and Exacerbations in Severe Asthma.
  Murphy RC, Morrell ED, Hallstrand TS.Am J Respir Crit Care Med. 2023 Feb 15;207(4):383-385. doi: 10.1164/rccm.202211-2074ED.PMID: 36413362 No abstract available.

Editorial

Am J Respir Crit Care Med

. 2023 Feb 15;207(4):388-389.
doi: 10.1164/rccm.202210-1870ED.

Interplay between Immune and Airway Smooth Muscle Cells in Obese Asthma

Anne E Dixon[1], Loretta G Que[2]
Affiliations expand

- PMID: 36219828
- DOI: 10.1164/rccm.202210-1870ED

No abstract available

Comment on

- Crosstalk between CD4+ T Cells and Airway Smooth Muscle in Pediatric Obesity-related Asthma.
  Yon C, Thompson DA, Jude JA, Panettieri RA Jr, Rastogi D.Am J Respir Crit Care Med. 2023 Feb 15;207(4):461-474. doi: 10.1164/rccm.202205-0985OC.PMID: 36194662

Am J Respir Crit Care Med
. 2023 Feb 15;207(4):461-474.
doi: 10.1164/rccm.202205-0985OC.

Crosstalk between CD4$^+$ T Cells and Airway Smooth Muscle in Pediatric Obesity-related Asthma

Changsuek Yon[1], David A Thompson[1], Joseph A Jude[2], Reynold A Panettieri Jr[2], Deepa Rastogi[1]
Affiliations expand

- PMID: 36194662
- DOI: 10.1164/rccm.202205-0985OC

Abstract

Rationale: Pediatric obesity-related asthma is a nonatopic asthma phenotype with high disease burden and few effective therapies. RhoGTPase upregulation in peripheral blood T helper (Th) cells is associated with the phenotype, but the mechanisms that underlie this association are not known. **Objectives:** To investigate the mechanisms by which upregulation of CDC42 (Cell Division Cycle 42), a RhoGTPase, in Th cells is associated with airway smooth muscle (ASM) biology. **Methods:** Chemotaxis of obese asthma and healthy-weight asthma Th cells, and their adhesion to obese and healthy-weight nonasthmatic ASM, was investigated. Transcriptomics and proteomics were used to determine the differential effect of obese and healthy-weight asthma Th cell adhesion to obese or healthy-weight ASM biology. **Measurements and Main Results:** Chemotaxis of obese asthma Th cells with CDC42 upregulation was resistant to CDC42 inhibition. Obese asthma Th cells were more adherent to obese ASM compared with healthy-weight asthma Th cells to healthy-weight ASM. Compared with coculture with healthy-weight ASM, obese asthma Th cell coculture with obese ASM was positively enriched for genes and proteins involved in actin cytoskeleton organization, transmembrane receptor protein kinase signaling, and cell mitosis, and negatively enriched for extracellular matrix organization. Targeted gene evaluation revealed upregulation of *IFNG*, *TNF* (tumor necrosis factor), and Cluster of Differentiation 247 (*CD247*) among Th cell genes, and of Ak strain transforming (*AKT*), Ras homolog family member A (*RHOA*), and *CD38*, with downregulation of *PRKCA* (Protein kinase C-alpha), among smooth muscle genes. **Conclusions:** Obese asthma Th cells have

uninhibited chemotaxis and are more adherent to obese ASM, which is associated with upregulation of genes and proteins associated with smooth muscle proliferation and reciprocal nonatopic Th cell activation.

Keywords: Th cells; airway smooth muscle; asthma; children; obesity.

Comment in

- Interplay between Immune and Airway Smooth Muscle Cells in Obese Asthma. Dixon AE, Que LG.Am J Respir Crit Care Med. 2023 Feb 15;207(4):388-389. doi: 10.1164/rccm.202210-1870ED.PMID: 36219828 No abstract available.

Am J Respir Crit Care Med

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. 2023 Feb 15;207(4):475-484.
doi: 10.1164/rccm.202203-0597OC.

Skeletal Muscle Adiposity and Lung Function Trajectory in the Severe Asthma Research Program

Matthew C Tattersall[1,2], Kristine E Lee[3], Nanae Tsuchiya[4,5], Fauzia Osman[2], Claudia E Korcarz[1,2], Kristin M Hansen[1,2], Michael C Peters[6], John V Fahy[6], Colin A Longhurst[2], Eleanor Dunican[7,8], Sally E Wentzel[9], Joseph K Leader[10], Elliot Israel[11,12], Bruce D Levy[11], Mario Castro[13], Serpil C Erzurum[14], Jason Lempel[15], Wendy C Moore[16], Eugene R Bleecker[17,18], Brenda R Phillips[19], David T Mauger[19], Eric A Hoffman[20,21,22], Sean B Fain[21], Scott B Reeder[3], Ron L Sorkness[23], Nizar N Jarjour[23,2], Loren C Denlinger[23,2], Mark L Schiebler[4]
Affiliations expand

- PMID: 36194556

- DOI: 10.1164/rccm.202203-0597OC

Abstract

Rationale: Extrapulmonary manifestations of asthma, including fatty infiltration in tissues, may reflect systemic inflammation and influence lung function and disease severity. **Objectives:** To determine if skeletal muscle adiposity predicts lung function trajectory in asthma. **Methods:** Adult SARP III (Severe Asthma Research Program III) participants with baseline computed tomography imaging and longitudinal postbronchodilator FEV_1% predicted (median follow-up 5 years [1,132 person-years]) were evaluated. The mean of left and right paraspinous muscle density (PSMD) at the 12th thoracic vertebral body was calculated (Hounsfield units [HU]). Lower PSMD reflects higher muscle adiposity. We derived PSMD reference ranges from healthy control subjects without asthma. A linear multivariable mixed-effects model was constructed to evaluate associations of baseline PSMD and lung function trajectory stratified by sex. **Measurements and Main Results:** Participants included 219 with asthma (67% women; mean [SD] body mass index, 32.3 [8.8] kg/m^2) and 37 control subjects (51% women; mean [SD] body mass index, 26.3 [4.7] kg/m^2). Participants with asthma had lower adjusted PSMD than control subjects (42.2 vs. 55.8 HU; $P < 0.001$). In adjusted models, PSMD predicted lung function trajectory in women with asthma (β = -0.47 Δ slope per 10-HU decrease; $P = 0.03$) but not men (β = 0.11 Δ slope per 10-HU decrease; $P = 0.77$). The highest PSMD tertile predicted a 2.9% improvement whereas the lowest tertile predicted a 1.8% decline in FEV_1% predicted among women with asthma over 5 years. **Conclusions:** Participants with asthma have lower PSMD, reflecting greater muscle fat infiltration. Baseline PSMD predicted lung function decline among women with asthma but not men. These data support an important role of metabolic dysfunction in lung function decline.

Keywords: longitudinal lung function; muscle adiposity; severe asthma.

. 2023 Feb 15;207(4):381-382.
doi: 10.1164/rccm.202209-1833ED.

Remodeling Phenotypes Take Center Stage in the Prediction of Preschool Wheeze Attacks

Sejal Saglani [1], Simonetta Baraldo [2]
Affiliations expand

- PMID: 36170640

- DOI: 10.1164/rccm.202209-1833ED

No abstract available

Comment on

- Bronchial Remodeling-based Latent Class Analysis Predicts Exacerbations in Severe Preschool Wheezers.
  Fayon M, Beaufils F, Esteves P, Campagnac M, Maurat E, Michelet M, Siao-Him-Fa V, Lavrand F, Simon G, Begueret H, Berger P; P'tit Asthme Study Group.Am J Respir Crit Care Med. 2023 Feb 15;207(4):416-426. doi: 10.1164/rccm.202205-0913OC.PMID: 36108144

supplementary info

Publication types, MeSH termsexpand

full text links

Editorial

Am J Respir Crit Care Med

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. 2023 Feb 15;207(4):385-386.
doi: 10.1164/rccm.202209-1768ED.

Bronchial Epithelial Cell CC16 mRNA: Novel Asthma Biomarker or the Same Book with a New Cover?

Brinda Desai[1], Praveen Akuthota[1]
Affiliations expand

- PMID: 36169926

- DOI: 10.1164/rccm.202209-1768ED

No abstract available

Comment on

- Low CC16 mRNA Expression Levels in Bronchial Epithelial Cells Are Associated with Asthma Severity.
  Li X, Guerra S, Ledford JG, Kraft M, Li H, Hastie AT, Castro M, Denlinger LC, Erzurum SC, Fahy JV, Gaston B, Israel E, Jarjour NN, Levy BD, Mauger DT, Moore WC, Zein J, Kaminski N, Wenzel SE, Woodruff PG, Meyers DA, Bleecker ER.Am J Respir Crit Care Med. 2023 Feb 15;207(4):438-451. doi: 10.1164/rccm.202206-1230OC.PMID: 36066606

supplementary info

Publication types, MeSH terms, Substancesexpand

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Am J Respir Crit Care Med

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. 2023 Feb 15;207(4):416-426.
doi: 10.1164/rccm.202205-0913OC.

Bronchial Remodeling-based Latent Class Analysis Predicts Exacerbations in Severe Preschool Wheezers

Michael Fayon[1 2 3], Fabien Beaufils[1 2 3], Pauline Esteves[1 3], Maryline Campagnac[1 3], Elise Maurat[1 3], Marine Michelet[4 5], Valerie Siao-Him-Fa[1 2 3], Frederic Lavrand[2], Guillaume Simon[2], Hugues Begueret[2], Patrick Berger[1 2 3]; P'tit Asthme Study Group
Collaborators, Affiliations expand

- PMID: 36108144

- DOI: 10.1164/rccm.202205-0913OC

Abstract

Rationale: Children with preschool wheezing represent a very heterogeneous population with wide variability regarding their clinical, inflammatory, obstructive, and/or remodeling patterns. We hypothesized that assessing bronchial remodeling would help clinicians to better characterize severe preschool wheezers. **Objectives:** The main objective was to identify bronchial remodeling-based latent classes of severe preschool wheezers. Secondary objectives were to compare cross-sectional and longitudinal clinical and biological data between classes and to assess the safety of bronchoscopy. **Methods:** This double-center prospective study (NCT02806466) included severe preschool wheezers (1-5 yr old) requiring fiberoptic bronchoscopy. Bronchial remodeling parameters (i.e., epithelial integrity, reticular basement membrane [RBM] thickness, mucus gland, fibrosis and bronchial smooth muscle [BSM] areas, the density of blood vessels, and RBM-BSM distance) were assessed and evaluated by latent class analysis. An independent cohort of severe preschool wheezers (NCT04558671) was used to validate our results. **Measurements and Main Results:** Fiberoptic bronchoscopy procedures were well tolerated. A two-class model was identified: Class BR1 was characterized by increased RBM thickness, normalized BSM area, the density of blood vessels, decreased mucus gland area, fibrosis, and RBM-BSM distance compared with Class BR2. No significant differences were found between classes in the year before fiberoptic bronchoscopy. By contrast, Class BR1 was associated with a shorter time to first exacerbation and an increased risk of both frequent (3 or more) and severe exacerbations during the year after bronchoscopy in the two cohorts. **Conclusions:** Assessing bronchial remodeling identified severe preschool wheezers at risk of frequent and severe subsequent exacerbations with a favorable benefit to risk ratio.

Keywords: asthma; bronchoscopy; child; exacerbation; latent class analysis.

Comment in

- Remodeling Phenotypes Take Center Stage in the Prediction of Preschool Wheeze Attacks.
  Saglani S, Baraldo S.Am J Respir Crit Care Med. 2023 Feb 15;207(4):381-382. doi: 10.1164/rccm.202209-1833ED.PMID: 36170640 No abstract available.

supplementary info

MeSH terms, Grant supportexpand

Am J Respir Crit Care Med
. 2023 Feb 15;207(4):438-451.
doi: 10.1164/rccm.202206-1230OC.

Low CC16 mRNA Expression Levels in Bronchial Epithelial Cells Are Associated with Asthma Severity

Xingnan Li[1], Stefano Guerra[2], Julie G Ledford[2], Monica Kraft[2], Huashi Li[1], Annette T Hastie[3], Mario Castro[4], Loren C Denlinger[5], Serpil C Erzurum[6], John V Fahy[7], Benjamin Gaston[8], Elliot Israel[9], Nizar N Jarjour[5], Bruce D Levy[9], David T Mauger[10], Wendy C Moore[3], Joe Zein[6], Naftali Kaminski[11], Sally E Wenzel[12], Prescott G Woodruff[7], Deborah A Meyers[1], Eugene R Bleecker[1]
Affiliations expand

- PMID: 36066606

- DOI: 10.1164/rccm.202206-1230OC

Abstract

Rationale: CC16 is a protein mainly produced by nonciliated bronchial epithelial cells (BECs) that participates in host defense. Reduced CC16 protein concentrations in BAL and serum are associated with asthma susceptibility. **Objectives:** Few studies have investigated the relationship between CC16 and asthma progression, and none has focused on BECs. In this study, we sought to determine if CC16 mRNA expression levels in BECs are associated with asthma severity. **Methods:** Association analyses between CC16 mRNA expression levels in BECs (242 asthmatics and 69 control subjects) and asthma-related phenotypes in Severe Asthma Research Program were performed using a generalized linear model. **Measurements and Main Results:** Low CC16 mRNA expression levels in BECs were significantly associated with asthma susceptibility and asthma severity, high systemic corticosteroids use, high retrospective and prospective asthma exacerbations, and low pulmonary function. Low CC16 mRNA expression levels were significantly associated with

high T2 inflammation biomarkers (fractional exhaled nitric oxide and sputum eosinophils). CC16 mRNA expression levels were negatively correlated with expression levels of Th2 genes (*IL1RL1*, *POSTN*, *SERPINB2*, *CLCA1*, *NOS2*, and *MUC5AC*) and positively correlated with expression levels of Th1 and inflammation genes (*IL12A* and *MUC5B*). A combination of two nontraditional T2 biomarkers (CC16 and IL-6) revealed four asthma endotypes with different characteristics of T2 inflammation, obesity, and asthma severity. **Conclusions:** Our findings indicate that low CC16 mRNA expression levels in BECs are associated with asthma susceptibility, severity, and exacerbations, partially through immunomodulation of T2 inflammation. CC16 is a potential nontraditional T2 biomarker for asthma development and progression.

Keywords: CC16; T2 inflammation; asthma exacerbations; asthma severity; bronchial epithelial cells.

Comment in

- Bronchial Epithelial Cell CC16 mRNA: Novel Asthma Biomarker or the Same Book with a New Cover?
  Desai B, Akuthota P.Am J Respir Crit Care Med. 2023 Feb 15;207(4):385-386. doi: 10.1164/rccm.202209-1768ED.PMID: 36169926 No abstract available.

RHINITIS

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Int Forum Allergy Rhinol
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. 2023 Feb 17.
doi: 10.1002/alr.23142. Online ahead of print.

Chronic intranasal corticosteroid treatment induces degeneration of olfactory sensory neurons in normal and allergic rhinitis mice

Pu Li[1], Na Wang[1], Luo Kai[2], Jinyuan Si[1], Zhenlin Wang[1]

Affiliations expand

- PMID: 36800514

- DOI: 10.1002/alr.23142

Abstract

Background: Nasal eosinophilic inflammation is the therapeutic target for olfactory dysfunction in allergic rhinitis (AR). Intranasal corticosteroids are commonly considered to offer targetable benefit given their immunosuppressive property. However, experimental evidence suggests that continuous corticosteroid exposure may directly cause olfactory damage by disrupting the turnover of olfactory sensory neurons (OSNs). This potentially deleterious effect of corticosteroids calls into question their long-term topical use for treating olfactory loss related to AR. The aim of this study was to assess the impacts of chronic intranasal corticosteroid treatment on olfactory function and OSN population in mice under normal and pathological conditions.

Methods: BALB/c mice were intranasally treated with fluticasone propionate (FP, 0.3 mg/kg) for up to 8 weeks. Additional mice were used to establish an ovalbumin-induced mouse model of AR, followed by nasal challenge with ovalbumin for 8 weeks in the presence or absence of intranasal FP treatment. We examined olfactory function, OSN existence, neuronal turnover, and nasal inflammation using the behavioral test, histological analyses, Western blotting, and enzyme-linked immunosorbent assay.

Results: Intranasal treatment with FP for 8 weeks (FP-wk8) reduced odor sensitivity in normal mice. This reduction was concomitant with loss of OSNs and the axons projecting to the olfactory bulb, primarily resulting from increased neuronal apoptosis. In FP-wk8 AR mice, intranasal FP treatment attenuated olfactory impairment and eosinophilic inflammation, but failed to reconstitute OSN population and axonal projections.

Conclusion: Our results suggest that chronic intranasal corticosteroid treatment contributes to OSN degeneration that may reduce the therapeutic effectiveness for AR-related olfactory loss. This article is protected by copyright. All rights reserved.

Keywords: allergic rhinitis; apoptosis; olfaction; olfactory sensory neurons; steroid therapy.

Review

Allergy

. 2023 Feb 17.
doi: 10.1111/all.15679. Online ahead of print.

Rhinitis associated with asthma is distinct from rhinitis alone: The ARIA-MeDALL hypothesis

J Bousquet[1 2 3 4], E Melén[5], T Haahtela[6], G H Koppelman[7], A Togias[8], R Valenta[9], C A Akdis[10], W Czarlewski[11 12], M Rothenberg[13], A Valiulis[14 15], M Wickmann[16], D Aguilar[17], M Akdis[10], I J Ansotegui[18], C Barbara[19], A Bedbrook[12], C Bindslev Jensen[20], S Bosnic-Anticevich[21 22], L P Boulet[23], C E Brightling[24], L Brussino[25 26], E Burte[4 27], M Bustamante[28 29], G W Canonica[30 31], L Cecchi[32], J C Celedon[33], C Chaves-Loureiro[34], E Costa[35], A A Cruz[36], M Erhola[37], B Gemicioglu[38], W J Fokkens[39], J Garcia Aymerich[28 29], S Guerra[40], J Heinrich[41], J C Ivancevich[42], T Keil[43 44 45], L Klimek[46 47], P Kuna[48], M Kupczyk[48], V Kvedariene[49 50], D E Larenas-Linnemann[51], N Lemonnier[52], K C Lodrup Carlsen[53], R Louis[54 55], M Makris[56], M Maurer[1], I Momas[57], M Morais-Almeida[58], J Mullol[59 60], R N Naclerio[61], K Nadeau[62], R Nadif[4 27], M Niedoszytko[63], Y Okamoto[64 65], M Ollert[20 66], N G Papadopoulos[67], G Passalacqua[68], V Patella[69 70], R Pawankar[71], N Pham-Thi[72], O Pfaar[73], F S Regateiro[74 75 76], J Ring[77 78], P W Rouadi[79 80], B Samolinski[81], J Sastre[82], M Savouré[4 27], N Scichilone[83], M H Shamji[84], A Sheikh[85], V Siroux[86], B Sousa-Pinto[87 88 89], M Standl[90], J Sunyer[28 29 91 92], L Taborda-Barata[93 94], S Toppila-Salmi[6], M J Torres[95], I Tsiligianni[96 97], E Valovirta[98 99], O Vandenplas[100], M T Ventura[101], S Weiss[102], A Yorgancioglu[103], L Zhang[104], A H Abdul Latiff[105], W Aberer[106], I Agache[107], M Al-Ahmad[108], I Alobid[109 110], H S Arshad[111 112], E Asayag[113], A Baharudin[114], L Battur[115], K S Bennoor[116], E C Berghea[117], K C Bergmann[1], D Bernstein[118], M Bewick[119], H Blain[120], M Bonini[121], F Braido[122], R Buhl[123], R Bumbacea[124], A Bush[125], M Calderon[126], G Calvo[127], P Camargos[128], L Caraballo[129], V Cardona[130 131], W Carr[132], P Carreiro-Martins[133 134], T Casale[135], A M Cepeda Sarabia[136], R Chandrasekharan[137], D Charpin[138], Y Z Chen[139], I Cherrez-Ojeda[140 141], T Chivato[142], E Chkhartishvili[143], G Christoff[144], D K Chu[145], C Cingi[146], J Correia da Sousa[147], C Corrigan[148], A Custovic[149], G D'Amato[150], S Del Giacco[151], F De Blay[152], P Devillier[153], A Didier[154], M do Ceu Teixeira[155], D Dokic[156], H Douagui[157], M Doulaptsi[158], S Durham[159], M Dykewicz[160], T Eiwegger[161], Z A El-Sayed[162], R Emuzyte[163], R Emuzyte[163], A Fiocchi[164], N Fyhrquist[165], R M Gomez[166], M Gotua[167], M A Guzman[168], J Hagemann[46], S Hamamah[169], S Halken[170], D M G Halpin[171], M Hofmann[1 172], E Hossny[162], M Hrubiško[173], C Irani[174], Z Ispayeva[175], E Jares[176], T Jartti[177], E Jassem[178], K Julge[179], J Just[180], M Jutel[181 182], I Kaidashev[183], O Kalayci[184], O Kalyoncu[185], P Kardas[186], B Kirenga[187], H Kraxner[188], I Kull[5], M Kulus[189], S La Gruta[190], S Lau[191], L Le Tuyet Thi[192], M Levin[193], B Lipworth[194], O Lourenço[195], B Mahboub[196], M J Mäkelä[6], E Martinez-Infante[197], P Matricardi[198], N Miculinic[199], N Migueres[152], F Mihaltan[200], Y Mohamad[201], M Moniusko[202], S Montefort[203], H Neffen[204], K Nekam[205], E Nunes[206], D Nyembue Tshipukane[207], R E O'Hehir[208], I Ogulur[10], K

Ohta[209], K Okubo[210], S Ouedraogo[211], H Olze[212], I Pali-Schöll[213], O Palomares[214], K Palosuo[215], C Panaitescu[216], P Panzner[217], H S Park[218], C Pitsios[219], D Plavec[220], T A Popov[221], F Puggioni[30], S Quirce[222], M Recto[223], R Repka-Ramirez[224], C Roballo-Cordeiro[225], N Roche[226,227], M Rodriguez-Gonzales[228], J Romantowski[63], N Rosario Filho[229], M Rottem[230], H Sagara[231], F Sarquis-Serpa[232], Z Sayah[233], S Scheire[234], P Schmid-Grendelmeier[235], J C Sisul[236], D Sole[237], M Soto-Martinez[238], M Sova[239], A Sperl[46], O Spranger[240], R Stelmach[241], C Suppli Ulrik[242], M Thomas[243], T To[244], A Todo-Bom[245], P V Tomazic[246], M Urrutia-Pereira[247], M Valentin-Rostan[248], E van Ganse[249], M Van Hage[250], T Vasankari[251,252], P Vichyanond[253], G Viegi[254], D Wallace[255], D Y Wang[256], S Williams[96], M Worm[257], P Yiallouros[219], P Yiallouros[219], O Yusuf[258], F Zaitoun[259], M Zernotti[260], M Zidarn[261,262], J Zuberbier[212], J A Fonseca[87,88,89], T Zuberbier[1,2], J M Anto[28,29,91,92]
Affiliations expand

- PMID: 36799120

- DOI: 10.1111/all.15679

Abstract

Asthma, rhinitis and atopic dermatitis (AD) are interrelated clinical phenotypes that partly overlap in the human interactome. The concept of "one-airway-one-disease", coined over 20 years ago, is a simplistic approach of the links between upper- and lower-airway allergic diseases. With new data, it is time to reassess the concept. This article reviews (i) the clinical observations that led to Allergic Rhinitis and its Impact on Asthma (ARIA), (ii) new insights into polysensitisation and multimorbidity, (iii) advances in mHealth for novel phenotype definition, (iv) confirmation in canonical epidemiologic studies, (v) genomic findings, (vi) treatment approaches and (vii) novel concepts on the onset of rhinitis and multimorbidity. One recent concept, bringing together upper- and lower-airway allergic diseases with skin, gut and neuropsychiatric multimorbidities, is the "Epithelial Barrier Hypothesis". This review determined that the "one-airway-one-disease" concept does not always hold true and that several phenotypes of disease can be defined. These phenotypes include an extreme "allergic" (asthma) phenotype combining asthma, rhinitis and conjunctivitis. Rhinitis alone and rhinitis and asthma multimorbidity represent two distinct diseases with the following differences: (i) genomic and transcriptomic background (Toll-Like Receptors and IL-17 for rhinitis alone as a local disease; IL-33 and IL-5 for allergic and non-allergic multimorbidity as a systemic disease), (ii) allergen sensitisation patterns (mono- or pauci-sensitisation versus polysensitisation), (iii) severity of symptoms and (iv) treatment response. In conclusion, rhinitis alone (local disease) and rhinitis with asthma multimorbidity (systemic disease) should be considered as two distinct diseases, possibly modulated by the microbiome, and may be a model for understanding the epidemics of chronic and auto-immune diseases.

Keywords: IL-17; IL-33; Toll-like receptors; asthma; microbiome; multimorbidity; rhinitis.

Int Arch Allergy Immunol
.
. 2023 Feb 16;1-9.
doi: 10.1159/000528987. Online ahead of print.

Prevalence and Clinical Characteristics of Patients with Moderate-to-Severe Asthma in Japan Using a JMDC Claims Database

Dong Wang[1], Chie Ito[1,2], Yuji Homma[2], Michinori Arimitsu[2], Hajime Yoshisue[1]
Affiliations expand

- PMID: 36796345
- DOI: 10.1159/000528987

Abstract

Introduction: Although the prevalence and burden of asthma are continuously increasing, there is a lack of evidence on the landscape of moderate-to-severe asthma in Japan. Here, we report the prevalence of moderate-to-severe asthma and describe patient's demographics and clinical characteristics from 2010 to 2019 using the JMDC claims database.

Methods: Patients (≥12 years) from the JMDC database with ≥2 asthma diagnoses in 2 different months in each index year were stratified as moderate-to-severe asthma based on the definition of asthma prevention and management guideline (Japanese Guidelines for Asthma, JGL) or Global Initiative for Asthma (GINA).

Primary objective: 10-year trend (2010-2019) in the prevalence of moderate-to-severe asthma.

Secondary objective: Demographics and clinical characteristics of patients from 2010 to 2019.

Results: Of 7,493,027 patients from the JMDC database, 38,089 and 133,557 were included in JGL and GINA cohorts, respectively, by 2019. Both cohorts presented an increasing trend in the prevalence rate of moderate-to-severe asthma from 2010 to 2019, irrespective of age groups. Demographics and clinical characteristics were consistent across the cohorts in each calendar year. Majority of patients were in the age group of 18-60 years in both JGL (86.6%) and GINA (84.2%) cohorts. Allergic rhinitis was the most frequent comorbidity and anaphylaxis the least frequent comorbidity reported in both the cohorts.

Conclusions: In Japan, the prevalence rate of patients with moderate-to-severe asthma, as per JGL or GINA in the JMDC database, increased from 2010 to 2019. The demographics and clinical characteristics were similar in both cohorts over the assessment duration.

Keywords: Asthma; Claims database; Clinical characteristics; Demographics; Prevalence.

4
Expert Rev Clin Immunol
. 2023 Feb 16.
doi: 10.1080/1744666X.2023.2181790. Online ahead of print.

Recent insights into comorbidities in atopic dermatitis

Caroline Gewiss[1], Matthias Augustin[1]
Affiliations expand

- PMID: 36796057
- DOI: 10.1080/1744666X.2023.2181790

Abstract

Introduction: The relationship between atopic dermatitis and atopic diseases such as food allergies, asthma, and allergic rhinitis in terms of co-occurrence, underlying mechanisms, and therapy is well documented. There is increasing evidence that atopic dermatitis is

associated with non-atopic comorbidities such as cardiac, autoimmune, and neuropsychological comorbidities, as well as cutaneous and extracutaneous infections, establishing atopic dermatitis as a systemic disease.

Areas covered: The authors reviewed evidence on atopic and non-atopic comorbidities of atopic dermatitis. A literature search was conducted in the PubMed for peer-reviewed articles published until October 2022.

Expert opinion: Atopic and non-atopic diseases co-exist with atopic dermatitis more often than would be expected by chance. The effect of biologics and small molecules on atopic and nonatopic comorbidities may contribute to a better understanding of the relationship between atopic dermatitis and its comorbidities. Their relationship needs to be explored further to dismantle the underlying mechanism and move toward an atopic dermatitis endotype-based therapeutic approach.

Keywords: atopic dermatitis; autoimmune; cardio-metabolic; comorbidities; cutaneous; eczema; extracutaneous; infections; neuropsychological; non-atopic.

Environ Res

. 2023 Feb 13;115455.
doi: 10.1016/j.envres.2023.115455. Online ahead of print.

Relationship of long-term air pollution exposure with asthma and rhinitis in Italy: an innovative multipollutant approach

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Affiliations expand

- PMID: 36791835

- DOI: 10.1016/j.envres.2023.115455

Abstract

Background: air pollution is a complex mixture; novel multipollutant approaches could help understanding the health effects of multiple concomitant exposures to air pollutants.

Aim: to assess the relationship of long-term air pollution exposure with the prevalence of respiratory/allergic symptoms and diseases in an Italian multicenter study using single and multipollutant approaches.

Methods: 14420 adults living in 6 Italian cities (Ancona, Pavia, Pisa, Sassari, Turin, Verona) were investigated in 2005-2011 within 11 different study cohorts. Questionnaire information about risk factors and health outcomes was collected. Machine learning derived mean annual concentrations of PM_{10}, $PM_{2.5}$, NO_2 and mean summer concentrations of O_3 ($\mu g/m^3$) at residential level (1-km resolution) were used for the period 2013-2015. The associations between the four pollutants and respiratory/allergic symptoms/diseases were assessed using two approaches: a) logistic regression models (single-pollutant models), b) principal component logistic regression models (multipollutant models). All the models were adjusted for age, sex, education level, smoking habits, season of interview, climatic index and included a random intercept for cohorts.

Results: the three-year average (± standard deviation) pollutants concentrations at residential level were: 20.3 ± 6.8 $\mu g/m^3$ for $PM_{2.5}$, 29.2 ± 7.0 $\mu g/m^3$ for PM_{10}, 28.0 ± 11.2 $\mu g/m^3$ for NO_2, and 70.9 ± 4.3 $\mu g/m^3$ for summer O_3. Through the multipollutant models the following associations emerged: PM_{10} and $PM_{2.5}$ were related to 14-25% increased odds of rhinitis, 23-34% of asthma and 30-33% of night awakening; NO_2 was related to 6-9% increased odds of rhinitis, 7-8% of asthma and 12% of night awakening; O_3 was associated with 37% increased odds of asthma attacks. Overall, the Odds Ratios estimated through the multipollutant models were attenuated when compared to those of the single-pollutant models.

Conclusions: this study enabled to obtain new information about the health effects of air pollution on respiratory/allergic outcomes in adults, applying innovative methods for exposure assessment and multipollutant analyses.

Keywords: Adults; Air pollutants; Asthma; Multipollutant approach; Observational study; Rhinitis.

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: Maria Beatrice Bilò had speaking and lecture fees supported by Astra Zeneca, GSK,

Novartis, Sanofi. The other authors have no competing financial interests or personal relationships to disclose.

Immunotherapy

. 2023 Feb 15.
doi: 10.2217/imt-2022-0215. Online ahead of print.

Real-world study: drug reduction in children with allergic rhinitis and asthma receiving immunotherapy

Jorge Sánchez [1], Leidy Alvarez [2], Elizabeth García [3]
Affiliations expand

- PMID: 36789565
- DOI: 10.2217/imt-2022-0215

Abstract

Background: The reduction of pharmacological treatment after allergen immunotherapy (AIT) for house dust mites (HDMs) has been little studied in children. **Objective:** To evaluate the reduction of pharmacological treatment comparing children that receive HDM immunotherapy (AIT group) versus only pharmacotherapy. **Methods:** A historic cohort of children with rhinitis or asthma was assessed. The main outcome was the frequency of complete drug discontinuation. **Results:** 100% drug reduction was higher for rhinitis (4-year cumulative incidence: 30 vs 10.7%) and asthma (24.1 vs 10.5%) in the AIT group (n = 987) than in the pharmacotherapy group (n = 2012). **Conclusion:** Immunotherapy is associated with a significant reduction of pharmacotherapy in children. This is a marker of clinical control and could be associated with positive economic impact.

Keywords: allergen; allergy; asthma; immunotherapy; mites; pharmacotherapy; real-life; real-word; rhinitis.

Plain language summary

The benefits of allergen immunotherapy for house dust mites has been little studied in children. The usefulness of this treatment in asthma over the use of pharmacotherapy has also not been clearly evaluated. The use of immunotherapy allowed greater reductions in pharmacological treatment in children with rhinitis and asthma. Immunotherapy is a useful treatment for childhood rhinitis and asthma and reduces the risk of adverse effects from pharmacological treatments.

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Acta Biomed

. 2023 Feb 13;94(1):e2023028.

doi: 10.23750/abm.v94i1.13474.

Effects of benralizumab in a population of patients affected by severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: a real life study

Carla Santomasi[1], Enrico Buonamico[2], Silvano Dragonieri[3], Lucia Iannuzzi[4], Andrea Portacci[5], Nicola Quaranta[6], Giovanna Elisiana Carpagnano[7]

Affiliations expand

- PMID: 36786266

- DOI: 10.23750/abm.v94i1.13474

Free article

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a frequent comorbidity in severe eosinophilic asthma (SEA), which may contribute to the loss of asthma control. CRSwNP and SEA share a T2-mediated mechanism and the use of some anti-asthma

monoclonal antibodies has recently been extended to CRSwNP. Unlike dupilumab and omalizumab, benralizumab approval for CRSwNP is ongoing. We aimed to evaluate the efficacy of benralizumab efficacy on SEA and on CRSwNP in patients affected by both pathologies in a real life setting.

Methods: 17 patients affected by both SEA and CRSwNP participated to our study. At baseline (T0) and at one year after benralizumab initiation (T1), all participants underwent spirometry, exhaled nitric oxide (FeNO), Asthma Control Test (ACT), nasal endoscopy with Nasal Polyp Score (NPS), nasal cytology and Sino-Nasal Outcome Test 22 (SNOT 22).The continuous oral corticosteroid therapy (OCS), the number of year exacerbations and the need for sinus surgery were also evaluated for each patient.

Results: At T1, a marked reduction of SNOT-22, NPS, nasal eosinophils and neutrophils count were shown compared to T0. Moreover, at T1 ACT was significantly increased and FeNO, exacerbations/year and mean OCS dosage were significantly reduced compared to T0.

Conclusions: Our real-life study demonstrates the efficacy of benralizumab not only on SEA but also on nasal cytology and on nasal polyposis, confirming that patients affected by both SEA and CRSwNP may receive a considerable benefit from anti-IL5 receptor, treating both the comorbidities at once.

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CHRONIC COUGH

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Review

HNO

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. 2023 Feb 16.
doi: 10.1007/s00106-023-01280-3. Online ahead of print.

[Current possibilities and challenges in the treatment of laryngopharyngeal reflux]

[Article in German]
Daniel Runggaldier[1,2], Bram van Schie[3,4], Silvan Marti[3,4], Jörg E Bohlender[3,4]
Affiliations expand

- PMID: 36795120

- DOI: 10.1007/s00106-023-01280-3

Abstract

in English, German

Laryngopharyngeal reflux (LPR) is characterized by backflow of gastric or gastroduodenal content and gases into the upper aerodigestive tract, which can damage the mucus membranes of the larynx and pharynx. It is associated with a variety of symptoms such as retrosternal burning and acid regurgitation, or other unspecific symptoms such as hoarseness, globus sensation, chronic cough, or mucus hypersecretion. Due to the lack of data and the heterogeneity of studies, diagnosis of LPR is problematic and challenging, as recently discussed. Moreover, the different therapeutic approaches are also discussed controversially in the face of the poor evidence base, and include pharmacologic and conservative dietary measures. Hence, in the following review, the available options for treatment of LPR are critically discussed and summarized for daily clinical use.

Keywords: Alginate; Laryngopharyngeal reflux; Mediterranean diet; Proton pump inhibitors; Refluxogenic diet score.

- 61 references

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Dev Med Child Neurol
.
. 2023 Feb 14.
doi: 10.1111/dmcn.15543. Online ahead of print.

User-perceived impact of long-term mechanical assisted cough in paediatric neurodisability

Brit Hov[1,2], Tiina Andersen[3,4], Michel Toussaint[5], Ingvild B Mikalsen[6,7], Maria Vollsaeter[7,8], Heidi Markussen[3,4], Solfrid Indrekvam[3,9], Vegard Hovland[1]
Affiliations expand

- PMID: 36787316

- DOI: 10.1111/dmcn.15543

Abstract

Aim: To (1) compare the perceived benefit of long-term mechanical insufflation-exsufflation (MI-E) of children with neuromuscular disorders (NMDs) and central nervous system (CNS) disorders, including health care needs and treatment routines and (2) describe the children's health-related quality of life (HRQoL).

Method: This cross-sectional study used a questionnaire and memory card data to assess the perceived benefit of MI-E via the Visual Analogue Scale (VAS; 10 maximum), willingness to pause treatment, level of health care needs before and after MI-E initiation, and the children's treatment routines. A DISABKIDS questionnaire assessed HRQoL (100 maximum).

Results: Seventy-three children using MI-E participated (42 males, median [interquartile range {IQR}] age 10 years 2 months [6 years 3 months-14 years 1 month]), 47 with NMDs (such as spinal muscular atrophy and Duchenne muscular dystrophy) and 26 with CNS disorders (such as cerebral palsy, encephalitis, neurometabolic and other diseases). The median (IQR) VAS score for the perceived benefit of MI-E therapy at stable state and respiratory tract infection were 9 (6-10) and 10 (8.5-10) respectively. Sixty-two per cent were reluctant or unwilling to pause MI-E therapy, with no NMD versus CNS disorder group difference. After MI-E initiation, fewer physician consultations and hospitalizations were reported by the group with NMDs. The MI-E routine was similar in both groups. The mean (SD) HRQoL score for 26 of 51 eligible children was 71 (16.7).

Interpretation: MI-E treatment was generally perceived as beneficial and performed equally in both diagnostic groups. HRQoL was in line with children with a moderate-to-severe chronic condition.

- 26 references

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Review

Zhonghua Jie He He Hu Xi Za Zhi

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. 2023 Feb 12;46(2):192-196.
doi: 10.3760/cma.j.cn112147-20220516-00411.

[Eosinophilic bronchitis: update and review]

[Article in Chinese]

W Z Zhan[1], K F Lai[1]

Affiliations expand

- PMID: 36740383

- DOI: 10.3760/cma.j.cn112147-20220516-00411

Abstract

in English, Chinese

Eosinophilic bronchitis (EB) is a common cause of chronic cough, which shares similar airway eosinophilic inflammation with asthma, however, there is no airway hyperresponsiveness and airflow obstruction. The mechanism of the different phenotype between EB and asthma remains unclear. The differences in the location of airway inflammation, the level of inflammatory mediators, the imbalance of important metabolic pathways, and the degree of airway remodeling may result in different pathogenesis

between EB and asthma. EB response well to inhaled corticosteroids but recurrence of EB is still high after treatment. The longer duration of treatment with inhaled corticosteroids could decrease the relapse rate. On the prognosis of EB, a long-term follow-up study suggested that EB should be a distinct entity rather than an early stage of asthma or chronic obstructive pulmonary disease.

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Review

Neuropharmacology

. 2023 Feb 15;224:109358.

doi: 10.1016/j.neuropharm.2022.109358. Epub 2022 Dec 1.

P2X receptors: Insights from the study of the domestic dog

Ronald Sluyter[1], Reece A Sophocleous[2], Leanne Stokes[3]

Affiliations expand

- PMID: 36464207

- DOI: 10.1016/j.neuropharm.2022.109358

Abstract

Fifty years ago, the late Geoffrey Burnstock described the concept of purinergic nerves and transmission bringing into existence the broader concepts of purinergic signaling including P2X receptors. These receptors are trimeric ligand-gated cation channels activated by extracellular adenosine 5'-triphosphate (ATP). P2X receptors have important roles in health and disease and continue to gain interest as potential therapeutic targets in inflammatory, neurological, cardiovascular and many other disorders including cancer. Current understanding of P2X receptors has largely arisen from the study of these receptors in

humans and rodents, but additional insights have been obtained from the study of P2X receptors in the domestic dog, Canis familiaris. This review article will briefly introduce purinergic signaling and P2X receptors, before detailing the pharmacological profiles of the two recombinant canine P2X receptors studied to date, P2X7 and P2X4. The article will then describe the current state of knowledge concerning the distribution and function of the P2X receptor family in dogs. The article will also discuss the characterization of single nucleotide polymorphisms in the canine P2RX7 gene, and contrast this variation to the canine P2RX4 gene, which is largely conserved between dogs. Finally, this article will outline published examples of the use of dogs to study the pharmacokinetics of P2X7 and P2X3 antagonists, and how they have contributed to the preclinical testing of antagonists to human P2X7, CE-224,535, and human P2X3, Gefapixant (AF-219, MK-7264) and Eliapixant (BAY, 1817080), with Gefapixant gaining recent approval for use in the treatment of refractory chronic cough in humans. This article is part of the Special Issue on 'Purinergic Signaling: 50 years'.

Keywords: Canine; Companion animal; Extracellular adenosine 5′-triphosphate; Ligand-gated ion channel; Purinergic receptor; Purinergic signaling.

QJM

. 2023 Feb 14;116(1):47-56.
doi: 10.1093/qjmed/hcac202.

Vaccination saves lives: a real-time study of patients with chronic diseases and severe COVID-19 infection

A Mukherjee [1], G Kumar [1], A Turuk [1], A Bhalla [2], T C Bingi [3], P Bhardwaj [4], T D Baruah [5], S Mukherjee [6], A Talukdar [7], Y Ray [8], M John [9], J R Khambholja [10], A H Patel [11], S Bhuniya [12], R Joshi [13], G R Menon [14], D Sahu [14], V V Rao [14], B Bhargava [1], S Panda [1]; NCRC Study Team

Collaborators, Affiliations expand

- PMID: 36053197
- PMCID: PMC9494346
- DOI: 10.1093/qjmed/hcac202

Free PMC article

Abstract

Objectives: This study aims to describe the demographic and clinical profile and ascertain the determinants of outcome among hospitalized coronavirus disease 2019 (COVID-19) adult patients enrolled in the National Clinical Registry for COVID-19 (NCRC).

Methods: NCRC is an on-going data collection platform operational in 42 hospitals across India. Data of hospitalized COVID-19 patients enrolled in NCRC between 1st September 2020 to 26th October 2021 were examined.

Results: Analysis of 29 509 hospitalized, adult COVID-19 patients [mean (SD) age: 51.1 (16.2) year; male: 18 752 (63.6%)] showed that 15 678 (53.1%) had at least one comorbidity. Among 25 715 (87.1%) symptomatic patients, fever was the commonest symptom (72.3%) followed by shortness of breath (48.9%) and dry cough (45.5%). In-hospital mortality was 14.5% (n = 3957). Adjusted odds of dying were significantly higher in age group ≥60 years, males, with diabetes, chronic kidney diseases, chronic liver disease, malignancy and tuberculosis, presenting with dyspnoea and neurological symptoms. WHO ordinal scale 4 or above at admission carried the highest odds of dying [5.6 (95% CI: 4.6-7.0)]. Patients receiving one [OR: 0.5 (95% CI: 0.4-0.7)] or two doses of anti-SARS CoV-2 vaccine [OR: 0.4 (95% CI: 0.3-0.7)] were protected from in-hospital mortality.

Conclusions: WHO ordinal scale at admission is the most important independent predictor for in-hospital death in COVID-19 patients. Anti-SARS-CoV2 vaccination provides significant protection against mortality.

supplementary info

MeSH terms, Grant supportexpand

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1
J Bras Pneumol
. 2023 Feb 13;49(1):e20220466.
doi: 10.36416/1806-3756/e20220466. eCollection 2023.

Tomographic pleuropulmonary manifestations in rheumatoid arthritis: a pictorial essay

[Article in English, Portuguese]

Guilherme das Posses Bridi[1], Márcio Valente Yamada Sawamura[2], Mark Wanderley[1], Luciana Volpon Soares Souza[3], Ronaldo Adib Kairalla[1,4], Letícia Kawano-Dourado[1,5,6], Bruno Guedes Baldi[1,7]
Affiliations expand

- PMID: 36790285
- DOI: 10.36416/1806-3756/e20220466

Free article

Abstract

Rheumatoid arthritis (RA) is an autoimmune inflammatory and heterogeneous disease that affects several systems, especially the joints. Among the extra-articular manifestations of RA, pleuropulmonary involvement occurs frequently, with different presentations, potentially in all anatomic thoracic compartments, and may determine high morbidity and mortality. The most common pleuropulmonary manifestations in patients with RA include interstitial lung disease (ILD), pleural disease, pulmonary arterial hypertension, rheumatoid lung nodules, airway disease (bronchiectasis and bronchiolitis), and lymphadenopathy. Pulmonary hypertension and ILD are the manifestations with the greatest negative impact in prognosis. HRCT of the chest is essential in the evaluation of patients with RA with respiratory symptoms, especially those with higher risk factors for ILD, such as male gender, smoking, older age, high levels of rheumatoid factor, or positive anti-cyclic citrullinated peptide antibody results. Additionally, other etiologies that may determine tomographic pleuropulmonary manifestations in patients with RA are infections, neoplasms, and drug-induced lung disease. In these scenarios, clinical presentation is heterogeneous, varying from being asymptomatic to having progressive respiratory failure. Knowledge on the potential etiologies causing tomographic pleuropulmonary manifestations in patients with RA coupled with proper clinical reasoning is crucial to diagnose and treat these patients.

Rheumatology (Oxford)

. 2023 Feb 15;kead077.
doi: 10.1093/rheumatology/kead077. Online ahead of print.

Clinico-radiological correlation and prognostic value of baseline chest computed tomography in eosinophilic granulomatosis with polyangiitis

Florence Delestre[1,2], Anne-Laure Brun[3], Benjamin Thoreau[1,2], Camille Taillé[2,4], Nicolas Limal[5], Xavier Puéchal[1,2], Luc Mouthon[1,2], Loïc Guillevin[1,2], Marie-Pierre Revel[2,6], Benjamin Terrier[1,2]
Affiliations expand

- PMID: 36790066

- DOI: 10.1093/rheumatology/kead077

Abstract

Objectives: While chest high-resolution computed tomography (HRCT) is correlated to severity and prognosis in asthma, it has not been studied in eosinophilic granulomatosis with polyangiitis. Our objective is to study the prognostic value of baseline high-resolution computed tomography in EGPA patients.

Methods: Retrospective, multicenter observational study in three French hospitals, including EGPA patients with available chest HRCT before any systemic treatment. Two experienced radiologists blind for clinical data evaluated HRCT images using semi-quantitative scoring. HRCT characteristics were correlated with clinical features and outcome.

Results: Among 46 patients, 38 (82.6%) had abnormal parenchymal findings on HRCT, including bronchial wall thickening (69.6%), mosaic perfusion (63.0%), ground-glass opacities (32.6%), bronchiectasis (30.4%), mucous plugging (21.7%) and consolidations (17.4%). Patients were clustered into three groups depending on HRCT features: ground-glass pattern i.e with ground-glass opacities with or without bronchial abnormalities (group 1, 28.3%), bronchial pattern (group 2, 41.3%), and extra-pulmonary pattern with no significant abnormality (group 3, 30.4%). Group 2 showed less frequent cardiac involvement (31.6 vs. 46.2 and 42.9% in groups 1 and 3), more frequent positive ANCA (52.6 vs. 0.0 and 14.3%) and higher eosinophil count (median 7,510 vs. 4,000 and 4,250/mm3). Group 1 showed worse prognosis with more frequent steroid-dependency (58.3 vs. 11.1 and 28.6%) and requirement for mepolizumab (25.0 vs. 11.1 and 7.1%). Conversely, group 2 showed a better outcome with higher rates of remission (88.9 vs. 41.6 and 71.4%).

Conclusion: Chest HRCT at diagnosis of EGPA may have prognostic value and help clinicians better manage these patients.

Keywords: Asthma; Eosinophilic granulomatosis with polyangiitis; High resolution computed tomography; Mepolizumab.

Transplant Proc

. 2023 Feb 12;S0041-1345(23)00019-2.
doi: 10.1016/j.transproceed.2023.01.004. Online ahead of print.

Pulmonary Carcinoid Tumorlet in the Explanted Lungs for Lung Transplantation: A Case Series of 15 Patients

Yuriko Terada[1], Ramsey R Hachem[2], Michael K Pasque[1], Hrishikesh S Kulkarni[2], Chad A Witt[2], Derek E Byers[2], Rodrigo Vazquez Guillamet[2], Ruben G Nava[1], Benjamin D Kozower[1], Bryan F Meyers[1], G Alexander Patterson[1], Daniel Kreisel[1], Varun Puri[1], Tsuyoshi Takahashi[3]
Affiliations expand

- PMID: 36781372

- DOI: 10.1016/j.transproceed.2023.01.004

Abstract

Background: Pulmonary carcinoid tumorlet (PCT) is defined as small proliferation of neuroendocrine cells that invade the adjacent basement membrane. It is often associated with chronic pulmonary inflammatory processes. However, the characteristics of PCT in end-stage lung diseases remain unclear.

Methods: We conducted a retrospective cohort study of the explanted lungs after transplantation at our institution between January 1999 and October 2020. Patients who underwent re-transplantation were excluded.

Results: Pulmonary carcinoid tumorlet was incidentally discovered in the explanted lungs from 15 patients (1.1%) out of 1367 lung transplants performed during the study period. Nine patients (60.0 %) were women, with a median age of 59 years (IQR: 57-62) at transplant. Underlying pulmonary indications for lung transplantation were chronic obstructive pulmonary disease (9/15, 60.0%), interstitial lung disease (2/15, 13.0%), pulmonary vascular disease (2/15, 13.0%), alpha-1 antitrypsin deficiency (1/15, 7.0%), and bronchiectasis (1/15, 7.0%). Of the patients who underwent bilateral lung transplantation (13/15, 86.7%), PCT was found in the right lung in 10 patients (10/13, 76.9%). Thirteen patients had one lesion, 1 patient had 2 lesions and 1 patient had multiple lesions.

Conclusion: Our study shows that PCT is generally uncommon, but when it occurs, it occurs more frequently on the right side and in female patients with end-stage pulmonary disease. Chronic obstructive pulmonary disease may be a predisposing factor for developing PCT.

Conflict of interest statement

DISCLOSURE 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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