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as a result of air trapping and hyperinflation. IC decreases further with activity and may correlate more strongly to exercise capacity than measures of airflow (FEV1). 6 minute walk test (6MWT) is an objective measurement of functional exercise capacity.

Objectives: The objectives were to examine the correlation between IC and exercise capacity using 6MWT (and FEV1 and exercise capacity) in COPD patients and to compare the correlation between IC and exercise capacity with FEV1 and exercise capacity in COPD patients.

Methods: This was a retrospective study. All COPD patients undergoing both 6MWT and spirometry and lung volumes in CGH from 1/1/2008 till 9/11/2011 were included.

Results: 144 subjects were included. Mean age (years) was 69.12(\pm 8.93). 138/144(96.5%) were male. Mean FEV1 (L) was 1.33(\pm 0.57). There was statistically significant correlation between FEV1 and 6MWT distance (simple linear regression coefficient, $r=28.99$, $p=0.021$, 95% confidence interval 4.42 to 53.57). After adjusting for cardiovascular disease, the correlation was still statistically significant($r=29.00$, $p=0.021$, 95% CI 4.36 to 53.63). There was statistically significant correlation between IC and 6MWT distance($r=38.81$, $p=0.003$, 95% CI 13.08 to 64.53). After adjusting for cardiovascular disease, correlation was still statistically significant($r=39.09$, $p=0.003$, 95% CI 13.22 to 64.96).

Conclusion: IC is better correlated with 6MWT distance (functional exercise capacity) ($p=0.003$) than FEV1(0.021) in COPD patients. Thus, we concluded from this study that IC is a better predictor of exercise capacity than FEV1 in COPD patients.

P2241

Comparison of validity of methacholine and mannitol bronchial challenges in asthma diagnosis

Konstantinos Porpodis, Kaliopi Domvri, Theodoros Kontakiotis, Dimitrios Latsios, Dimitrios Ioannidis, Pashalina Giouleka, Konstantinos Zarogoulidis, Despoina Papakosta. *Department of Pneumology, Aristotle University of Thessaloniki, Hospital "G. Papanicolaou", Exochi, Thessaloniki, Greece*

Background: Detection of BHR with methacholine or mannitol have been highly sensitive tests to identify asthma diagnosis.

Purpose: The purpose of this study was to demonstrate the diagnostic validity of the two bronchial challenges and their correlation with symptoms, atopy and inflammatory markers.

Methods: Eighty-eight patients, 47 women and 41 men, aged 14-75 years who presented with asthma related symptoms and were not on any anti-asthma medication, were challenged with mannitol and methacholine. Medical history, physical examination, skin prick tests, Asthma Control Test (ACT) and FeNO levels were also assessed. The clinical diagnosis of asthma was based on bronchodilator reversibility test.

Results: Sixty seven patients were diagnosed with asthma and 21 without asthma. Both methacholine ($p<0.014$) and mannitol ($p<0.000$) challenges were significant in diagnosing asthma. The sensitivity/specificity was 62.68%/85.71% for methacholine, 64.17%/95.23% for mannitol and 64.70%/93.75% for both methods together, whereas the positive/negative predictive value was 93.33%/41.86%, 97.72%/45.45% and 97.05%/45.45%, respectively. There was a negative correlation between PC20 of methacholine and the FeNO level $p<0.001$, and positive with the PD15 of mannitol $p<0.001$ and the pre-test FEV1% pred $p<0.005$, whereas PD15 of mannitol was negatively correlated with the FeNO level $p<0.001$. Furthermore, dyspnoea was the only asthmatic symptom associated with FeNO level $p<0.035$ and the positivity of mannitol $p<0.014$ and methacholine $p<0.04$.

Conclusions: Both provocation methods were equivalent in diagnosing asthma, although sensitivity/specificity values appeared to be slightly higher in mannitol challenge.

P2242

Repeatability of peak nasal inspiratory flow rate (PNIF) measurements and its change after administration of 0.05% oxymetazoline

Anna Dor-Wojnarowska¹, Jerzy Liebhart¹, Marek Rabski¹, Andrzej Fal¹, Bernard Panaszek¹, Boleslaw Samolinski², Rafal Dobek¹. ¹Internal Medicine, Geriatriy and Allergology, Wroclaw Medical University, Wroclaw, Poland; ²Department of Prevention of Environmental Hazards and Allergology, Warsaw Medical University, Warsaw, Poland

Background: Measurement of PNIF is a cheap and easily performed method to assess nasal patency. However, the assessment of repeatability of this parameter as well as the threshold value of change which can be considered significant have not been established yet.

The aim of this study was to assess the repeatability of PNIF measurements and its change after the administration of 0.05% oxymetazoline.

Methods: Repeated measurements of PNIF (In-Check's Clement-Clark) were performed in 333 (174 women) healthy volunteers. Subjects were divided into three age groups (6-7, 13-14 and 20-45 years). Each subject carried out 5 measurements. PNIF was retaken 30 minutes after inhaling 0.05% oxymetazoline in 294 subjects. The variability of the PNIF was assessed using the coefficient of variation (CV=standard deviation x 100%/mean).

Results: The first four PNIF measurements significantly differed from each other. There was no statistically significant difference only between the fifth and fourth

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P2240

Is inspiratory capacity (IC) better correlated with functional exercise capacity than FEV1 in COPD patients?

Hang Siang Wong¹, Hwee Lee Ng¹, Corrine Bee Lay Kang². ¹Respiratory Medicine, Changi General Hospital, Singapore, Singapore; ²Clinical Measurement Unit, Changi General Hospital, Singapore, Singapore

Introduction: In COPD, resting residual volume is increased and IC is decreased

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measurement ($p=0.19$). PNIF repeatability was found at the acceptable level; the median value of CV was 15.5% (0-66), and it did not vary significantly between age groups. Statistically significant increases in PNIF value by 14.3% (-45, 157%) was observed the after administration of 0.05% oxymetazoline ($p=0.000000$)

Conclusions: 1. Only the PNIF value from the 4th and 5th sample did not differ significantly, thus at least 3 measurements are needed.

2. The PNIF is satisfactorily characterized by a relatively low coefficient of variation (15%).

3. The administration of oxymetazoline 0.05% causes an increase in PNIF by approximately 14% from the baseline value.

P2243

Detection of air leaks and their effects on forced oscillometry measurements

Andras Bikov^{1,2}, Omar Usmani¹, Neil Pride¹, James Hull¹, Ildiko Horvath², Peter Barnes¹, Paolo Pardi¹. ¹Airway Disease, National Heart and Lung Institute, Imperial College, London, United Kingdom; ²Department of Pulmonology, Semmelweis University, Budapest, Hungary

Introduction: Forced oscillation technique (FOT) is a method to estimate respiratory resistance (Rrs) and reactance (Xrs). However, some common artefacts may affect the accuracy of FOT readings. In particular, air leaks from lips not sealed around the mouthpiece, or those from the equipment. We studied the significance of this artefact and identified possible markers to detect it.

Methods: 11 healthy subjects (33 ± 7 years) underwent FOT measurements (Jaeger, Wurzburg, Germany) which generated 0.4 kPa peak-to-peak input signals. The Rrs and Xrs values at 5 and 20 Hz (R5, R20, X5) were registered in parallel with breathing volumes. To simulate air leaks, we applied artificial holes of increasing sizes (3.5 mm, 6 mm, and 8.5 mm diameters) on the breathing filter at 1 cm from the circumference. FOT data were compared to normal values obtained with no air leaks.

Results: With increasingly bigger filter holes and resulting air leaks, we identified corresponding larger indentations in the descending limb of the breathing volume (ΔV (2.2 ± 0.6 mL, 5.3 ± 1.7 mL, 8.7 ± 3.1 mL and 14.4 ± 2.9 mL; respectively, $p < 0.001$), indicating that ΔV may be a marker for air leak. This was confirmed by a significant correlation between ΔV and R5 ($p < 0.001$, $r = -0.74$), R20 ($p < 0.001$, $r = -0.71$), X5 ($p < 0.001$, $r = -0.79$) and R5-R20 ($p = 0.001$, $r = -0.50$). In line with this, a 1.1 mL increase in ΔV was associated with a 10% decrease in R5 values.

Conclusion: Indentations on the descending limb of the breathing volume may be used to detect the presence and magnitude of air leaks. Visual inspection of the data is required to exclude records where indentations are found.

The first author is receiving an ERS Long Term Fellowship.

P2244

Early diagnosis of small airway disease

Evangelia Daniil, Georgios Katsakos, Sofia-Antiopi Gennimata, Anastasios Palamidis, John Jordanoglou, Nikolaos G. Koulouris. 1st Respiratory Medicine Dept, Athens University, Sotiria Hospital, Athens, Attica, Greece

Inflammatory changes in the peripheral airways of smokers are detected even when "normal" spirometry is still present, indicating that early structural damage in the small airways develop before the diagnosis of overt COPD is established. There are several tests, as FEF_{25-75%}, slope of phase III, and effective time (Thorax 1980; 35: 375-378) and its variations, advocated to early detect small airways disease and discriminate between smokers and non-smokers. However, it is not clear which of the aforementioned tests is the "best" for early detection of small airways disease. We studied 30 (15 men) Caucasian subjects (10 never smokers, 10 smokers with normal spirometry, and 10 COPDers in GOLD I), aged (mean \pm SD) 52 ± 14 y with FVC%pred = 111 ± 12 , FEV₁%pred = 98 ± 14 , FEV₁/FVC% = 73 ± 10 . All smokers had smoking history more than 10 pack-years. Simple spirometry, the slope of phase III ($\Delta N_2/I$), and the effective time at the 60-70% part of the forced vital capacity of the lung (TEFF₇) were measured. The FEF_{25-75%}%pred (64 ± 29) was abnormal in 16/30 subjects. The $\Delta N_2/I$ %pred (192 ± 150) was abnormal in 14/30 subjects. TEFF₇%pred was 155 ± 88 and was abnormal in 17/30. Multiple linear regression analysis showed that TEFF₇%pred is more appropriate, among the tests performed, for discriminating smokers from never smokers ($p = 0.008$). In conclusion, TEFF₇ appears to be a sensitive test for the early detection of small airway disease.

P2245

Prognostic factors in COPD patients controlled in two outpatient clinics

Verónica Hernández, Patricia Sobradillo, Laura Tomás, Laura Cancelo, Francisco Javier Ribas, Mikel Azpiroz, Vanesa Zorrilla, Begoña Lahidalga, José Luis Lobo. Respiratory, HUA - Txagorritxu, Vitoria - Gasteiz, Araba, Spain

FEV1 and a number of composite indexes (BODE, U-BODE, ADO) predict mortality in the population of patients with chronic obstructive pulmonary disease (COPD) at large. However, patients attending the specialized clinics of tertiary referral hospitals are often old and suffer severe or very severe airflow limitation. We aimed to compare the prognostic value of FEV1, BODE, U-BODE and ADO indexes in patients attending the outpatient clinics of Hospital de Cruces, a tertiary referral hospital in Bilbao (Spain).

Patients from two outpatient clinics were included. FEV1, BODE, U-BODE and

ADO values were determined at recruitment and patients were followed up for a mean of 4.5 years.

We studied 106 patients (70.5 ± 8.9 yrs.; FEV1 $44.4 \pm 9.9\%$ of ref.), 35 of whom (33%) died during follow-up. In this population, FEV1 did not predict mortality, whereas BODE ($p = 0.001$), U-BODE ($p = 0.000$) and ADO indexes ($p = 0.003$) did. BMI did not discriminate survival significantly but dyspnea ($p = 0.003$), distance walked ($p = 0.000$) and age ($p = 0.02$) did.

In patients attending the outpatient clinic of a tertiary referral hospital, FEV1 is not a good prognostic marker, at variance to age, dyspnea, walked distance, ADO, BODE and U-BODE indexes.

P2246

Evaluation of treatment with fixed dose combinations in asthma patients in primary care in Sweden by using mannitol challenge test

Kerstin Romborg^{1,2}, Anna-Carin Berggren³. ¹Health Care Centre, Näsets läkargrupp, Höllviken, Sweden; ²Department of Respiratory Medicine and Allergology, Department of Clinical Science, Lund University, Lund, Sweden; ³Medical Department, Mundipharma AB, Göteborg, Sweden

Background: The mannitol challenge test is an indirect bronchial challenge test suitable for use in a primary-care setting. The test is most often used to diagnose asthma. In this pilot study the test was used to evaluate the effectiveness of ongoing treatment with ICS/LABA combination therapy in patients with asthma.

Objectives: To explore the prevalence of optimal treated asthma patients in primary care in Sweden. The hypothesis was that not all patients are optimally treated.

Methods: Male and female subjects, age 18-65 years with asthma, who were treated with a fixed dose combination (budesonide/formoterol or fluticasone/salmeterol) were included in the study. The subjects performed a mannitol challenge test (direct fall) followed by an inhalation of a β_2 -agonist. A new spirometry (reversibility test) was performed 15 minutes later. The main explorative end-point was positive or negative response of mannitol challenge test and/or a reversibility of $\geq 15\%$.

Results: The preliminary result of this pilot study (100 subjects) shows that an unexpected, surprisingly high proportion of the asthma patients had a positive response, either as a direct fall of FEV₁ $\geq 15\%$ in the mannitol challenge test and/or a reversibility of $\geq 15\%$.

Conclusion: The result of this study indicates that a large proportion of asthma patients in primary care, who are currently treated with fixed dose combination therapy, may not be optimally treated. Further research is needed to support these findings and to understand the reasons.

P2247

Difference of respiratory reactance between mild and moderate COPD by forced oscillation technique using a MostGraph-01

Yasuhiro Yamauchi, Tadashi Kohyama, Taisuke Jo, Masafumi Horie, Yuu Mikami, Takahide Nagase. Respiratory Medicine, The University of Tokyo, Japan

Background: COPD is characterized with persistent airflow limitation caused by airway inflammation and parenchymal emphysema. The Forced Oscillation Technique (FOT) can detect the lung impairment by measuring respiratory impedance during tidal breathing without special maneuver of respiration. Respiratory impedance consists of resistance and reactance (Xrs), which dynamically change during tidal breathing in COPD patients. We evaluated the difference of the Xrs in respiratory cycle between mild and moderate COPD.

Methods: We recruited 26 outpatients with stable mild ($n=13$) and moderate ($n=13$) COPD at the University of Tokyo Hospital. The impedance of respiratory system was measured by FOT using MostGraph-01, which was manufactured in Japan CHEST Company. The Xrs during inspiratory and expiratory phase during tidal breathing were evaluated at 4 Hz of oscillatory frequency. Comparisons of Xrs between both groups were performed using the Student's t-test.

Results: The mean Xrs at 4 Hz (X4) in respiratory cycle were similar in mild and moderate groups. There were also no significant differences between inspiratory X4 (insX4) and expiratory X4 (exX4) in both groups. However, the ratio of insX4 to exX4 in mild COPD was significantly lower than that in moderate COPD ($p=0.031$).

Conclusion: The ratio of insX4 to exX4 during tidal breathing in mild COPD was lower than moderate COPD. During tidal breathing, the Xrs changes in inspiratory and expiratory phase and might be influenced by airway obstruction and parenchymal emphysematous change. The measurement of Xrs during tidal breathing might be useful property to distinguish the severity of COPD.

P2248

Mannitol challenge testing in clinical practice and its role in identifying always hyperreactivity

Alison Gill, Ian Clifton. Department of Respiratory Medicine, St. James' University Hospital, Leeds, United Kingdom

Introduction: Mannitol challenge testing can be useful in asthma diagnosis, to demonstrate objective evidence of airways hyperreactivity (AH).

Aim: To review mannitol testing locally, identify characteristics of those with positive and negative tests, and look at outcomes in terms of diagnosis and clinical improvement.

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Methods: We reviewed all tests in our Trust between 2009 and 2011, compared baseline spirometry between positive and negative tests, and looked at immunological evidence of atopy. We reviewed clinic letters for change in diagnosis or management, as well as symptomatic improvement and whether patients were discharged from follow-up (representing clinical stability).

Results: Tests were performed on 177 patients between April 2009 and October 2011. The positive and negative groups were compared in terms of spirometry and immunological evidence for atopy (total IgE and IgE to inhaled allergen mix and aspergillus). The test was positive in 40 patients (22.6%). Of these, immunological evidence of atopy was greater than in those with negative tests (mean total IgE 275 vs. 132; IgE to IAM 5.48 and 4.73; IgE to aspergillus 0.6 and 0.25 respectively). Baseline spirometry tended towards more airflow obstruction in the positive group though the means were both within normal range (89% and 97% predicted). Of the 126 patients for whom we had data the mannitol challenge resulted in changes in treatment and improved symptoms in 115 (91.2%).

Conclusion: Bronchial provocation testing is useful in identifying those with AH, and for guiding treatment leading to symptomatic improvement.

P2249

Best time for evaluating the response to bronchodilators

Abouda Maher, El Goul Jamel, Youngui Ferdaous, Triki Miriam, Charfi Med Ridha. *Pneumology, FSI, La Marsa, Tunis, Tunisia*

Introduction: There is no clear consensus on the time of interpretation of the bronchodilator effect. The interval between administration of bronchodilator type β_2 -agonist short-acting and the practice of post bronchodilator spirometry remains a controversial issue. Our objective was to define the optimal time of bronchodilator responsiveness in assessing the reversibility or otherwise of an obstructive respiratory disorder (ORD).

Materials and methods: Analytical study prospectively over a period of 8 months, performed in the pneumology service of FSI Hospital Security. The study included patients with ORD defined by an FEV₁/FVC <0.7 and who had consulted outside of an exacerbation. Flows and expiratory volumes (FEV, FVC) were measured before and after bronchodilator in the 5th, 10th, 15th, 20th and 30th minute. The response to BD was expressed in absolute and percentage change from baseline.

Results: 58 patients were included in the study, mean age 54±15 years with a majority of men. Our study was conducted in patients with asthma and COPD whose airway obstruction was moderate (FEV = 2 liters, or 62±15% predicted). (1) The maximum response after bronchodilator occurred at the 20th and 30th minutes respectively for FVC and FEV. (2) The number of reversible patients was guideline depending. (3) The maximum number of reversible patients was obtained in the 20th minute with a significant difference compared to that observed at the 5th and 10th minute.

Conclusion: The interpretation of the response to bronchodilator in the 20th minute after was the ideal time to assess the reversibility of ORD.

P2250

Small airway dysfunction by impulse oscillometry system (IOS) in asthma.

Relationship with spirometry, bronchodilator response and disease control

Roberta Pisi, Panagiota Tzani, Marina Aiello, Enrico Martinelli, Emilio Marangio, Dario Olivieri, Alfredo Chetta. *Clinical Sciences Dpt, Respiratory Disease Unit, University Hospital, Parma, Italy*

Rationale: Small airways are relevant to the pathophysiology of asthma

Objective: We investigated the relationship between small airway function, as assessed by IOS and spirometry, bronchodilator response, disease control and fractional exhaled nitric oxide (FeNO) values, in asthmatic patients.

Methods: We studied 38 patients with asthma (24 F, age range 16-70 yr). The fall in resistance from 5 to 20 Hz (R5-R20) and reactance at 5 Hz (X5) in kPa s l⁻¹ by IOS and spirometry at baseline and after 400 mcg of salbutamol were measured. Asthma Control Test (ACT) and FeNO (in ppb) were also recorded.

Results: R5-R20 and X5 were significantly related to spirometry, with FEF₂₅₋₇₅ being the parameter stronger related. By the ROC curve method, the FEF₂₅₋₇₅ cut-off point, which better identified patients with an increase in R5-R20 was ≤ 38% of pred (0.95 sensitivity and 0.78 specificity). When the bronchodilator responses were considered, only the post-bronchodilator FEV₁ percent changes correlated to the corresponding R5-R20 values ($p < 0.05$). ACT score, but not FeNO values was related to R5-R20 ($p < 0.001$) and X5 ($p < 0.01$) values. Logistic regression analysis showed that increased R5-R20 was independently associated with poor controlled asthma ($p < 0.05$).

Conclusions: We found that R5-R20 and X5 were related to FEF₂₅₋₇₅, as baseline values but not as percent change after bronchodilator. The increase in peripheral airway resistance was associated with a poor asthma control, but not with FeNO values. These results further confirm the value of IOS as investigative tool in asthma.

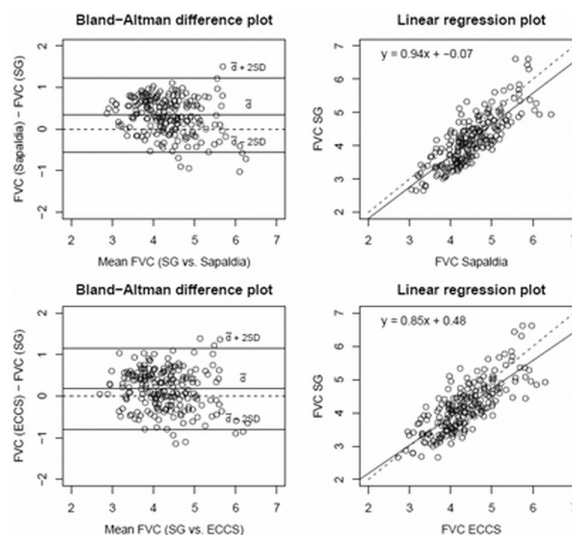
P2251

Comparison of SAPADIA and ECCS lung function normal values in a Swiss hospital setting

Jochen Rüdiger¹, Florent Baty¹, Andreas Bloch¹, Lukas Kern², Tino Schneider¹, Martin Brutsche¹. ¹Pneumologie, Kantonsspital St. Gallen, St. Gallen, Switzerland; ²Pneumologie, Zuger Kantonsspital AG, Baar, Switzerland

The SAPADIA survey observed better lung function in healthy volunteers than the common ECCS normal values (ECCS) predicted. We thus introduced the SAPADIA normal values (SAP) for lung function interpretation at the Kantonsspital St. Gallen. We currently analyzed the distribution of FVC and FEV₁ in non-pulmonary patients with a normal lung function comparing SAP and ECCS (so far 379 lung functions). Data was analyzed using descriptive statistics, Bland-Altman (BA) analysis and linear regression. Estimated bias and precision were calculated.

For FEV₁ we observed a significant difference between ECCS and SAP only in elderly men (>59 y.o.) (7±336 vs. 122±336 ml/s). When comparing FVC using SAP, the Bland Altman analysis revealed a bias, which was significantly lower using ECCS (e.g. in men bias of SAP was 0.33 l (0.27-0.39), bias of ECCS was 0.18 l (0.11-0.24), (fig.1, lower panels).



In summary, SAP tended to overestimate FVC and FEV₁ in elderly men compared to ECCS. However, absence of a pulmonary consultation in our population does not exclude a slight impact of the underlying disease on lung function.

We consider SAP for FEV₁ and FVC appropriate for the measurement of lung function of our population. Cut-off values require special attention especially in elderly.

P2252

Prevalence of hyperinflation and its reversibility in asthma patients with poorly controlled disease or significant dyspnea

Thierry Perez¹, Pascal Chanez², Daniel Dusser³, Daniel Vesque⁴, Philippe Devillier⁵. ¹Service Clinique des Maladies Respiratoires, CHRU de Lille - Hôpital Albert Calmette, Lille, France; ²Département des Maladies Respiratoires, AP-HM, Laboratoire d'immunologie INSERM CNRS U 600, UMR6212, Université de la Méditerranée, Marseille, France; ³Service Pneumologie, Hôpital Cochin - Groupement Hospitalier Universitaire Ouest - APHP, Paris, France; ⁴Direction des Affaires Médicales, Laboratoire Chiesi SA, Courbevoie, France; ⁵UPRES EA 220, Hôpital Foch, Suresnes, France

Introduction: Inflammation in asthma involves proximal and distal airways. The latter may induce a significant hyperinflation (HI).

Aim: To evaluate the prevalence of HI by body plethysmography in asthmatic patients with poorly controlled disease and/or significant dyspnea.

Methods: In 324 patients (age 49±17; FEV₁ 75±18% pred) insufficient asthma control was defined by an ACT score < 20 (n = 302) or a significant dyspnea by a MRC score ≥ 1 (n=22).

HI was defined by either a RV > pred + 1.64 RSD (=RV-HI) or a FRC > 120% pred (=FRC-HI). HI reversibility after bronchodilator was defined by a decrease of RV > 20% or a reduction of FRC > 10% from baseline. Change in dyspnea and chest tightness were evaluated by a VAS.

Results: HI was found in 49% (RV-HI) and 47% (FRC-HI) of cases. Prevalence of HI was higher in patients with a FEV₁ < 60% pred than in those with a FEV₁ > 80% pred: 78% for RV-HI and 70% for FRC-HI, vs 34% and 40%, respectively. ACT score was lower in patients with FRC-HI (13.4±4 vs 14.6±4; p = 0.004). Post-bronchodilator change was -10±13% for FRC, and -12±21% for RV. HI reversibility was obtained in 59% of cases with RV-HI and 47% of cases with FRC-HI. Chest tightness decrease after bronchodilator was greater in patients with

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baseline FRC-HI (-44±25 vs -37±24 mm, $p = 0.02$). Dyspnea improvement was higher in those with baseline RV-HI (-45±26 mm vs -38±23, $p = 0.02$).

Conclusion: Hyperinflation is frequent in poorly controlled asthma, including patients with normal FEV₁, suggesting an involvement of distal airways. It appears reversible in more than half of cases.

P2253

Spirometry and home oxygen in COPD patients with and without a history of illicit drug smoking

Andrew Singer, Nicola Garner, Janet Bonner, Tracy Monaghan, Hassan Burhan. Respiratory, Royal Liverpool University Hospital, Liverpool, United Kingdom

Our 960 bed inner city hospital has 3 full time COPD nurses providing a 7-day a week service reviewing patients admitted with COPD exacerbations. They are employed with a view to reducing length of stay and preventing re-admissions. The team audited their work prospectively.

Several patients have recurrent admissions with exacerbations of COPD. We looked at the database from January 2009 to September 2011 and compared spirometric confirmation of COPD and home oxygen prescription amongst four groups of patients: Ex-tobacco smokers and active tobacco smokers with and without a history of illicit drug smoking.

Results:

	No history of drug use	History of Drug Use
Average Age (yrs)	70	53.9
Number of Admissions	1114	252
Home oxygen (%)	244 (22)	59 (23)
Spirometry (%)	489 (44)	118 (47)

	No history of drug use		History of Drug Use	
	Ex-Tobacco Smokers	Active Tobacco Smokers	Ex-Tobacco Smokers	Active Tobacco Smokers
Average Age (yrs)	71.3	68.4	57.3	53.1
Number of Admissions	607	507	42	210
Home oxygen (%)	100 (22)	13 (22)	20 (48)	39 (19)
Spirometry (%)	242 (40)	247 (49)	20 (48)	98 (46)

Conclusion: There were no significant differences in the proportion of patients that had documented spirometry or a home oxygen prescription amongst those with and without a history of illicit drug smoking. A greater proportion of ex-smokers with a history of illicit drug smoking had a home oxygen prescription. This may reflect more severe disease which may be caused by the additional damage caused by drug smoking.

P2254

Assessment of ventilation heterogeneity by impulse oscillometry in patients with mild asthma

Gakuva Tamagaki, Hiroshi Kanazawa, Yukari Kon, Naoko Yoshii, Yukikazu Ichimaru, Kazuhisa Asai, Yoshihiro Tochino, Kazuto Hirata. Respiratory Medicine, Osaka City University, Osaka, Japan

Ventilation heterogeneity is an independent determinant of airway hyperresponsiveness (AHR) in asthma, and its measurement is complex and technically difficult. Impulse oscillometry (IOS) is increasingly used to obtain information on the state of the respiratory system. In this study, we determined the clinical validity of IOS as a novel and simple method for the assessment of ventilation heterogeneity in asthma.

Serial measurement of resistance at 5 Hz (R5) or 20 Hz (R20) by IOS was performed in 23 mild asthmatic patients and 28 normal control subjects; the measurements were made at baseline, after methacholine (maximal dose) provocation test for asthma and subsequent salbutamol administration. Further, exhaled nitric oxide (eNO) levels were examined and pulmonary function test was also performed.

The baseline R5, but not R20, was significantly higher in asthmatic patients than in controls. Both R5 and R20 were not significantly correlated with the degree of airway obstruction and eNO levels. However, R5 was significantly correlated with the severity of AHR ($r = -0.55$, $P = 0.01$), whereas R20 was not. The change in

forced expiratory volume in 1 s (FEV₁) (mean, 30%) after methacholine challenge was almost similar to the change in R20 (20%). However, the change in R5 (77%) after methacholine challenge was significantly greater than the change in FEV₁, and this finding is consistent with its greater sensitivity to airway dilated responses after salbutamol administration.

The proportional change in R5 after methacholine and salbutamol administration is attributable to variable small airway functions, suggesting that R5 may potentially represent ventilation heterogeneity in asthma patients.

P2255

Heterogeneity of small airways flow and hyperinflation are markers of a persistent obstruction phenotype in severe non-controlled asthmatics

Regina Maria Carvalho-Pinto, Alberto Cukier, Luciene Angelini, Frederico Leon Arrabal Fernandes, João Marcos Salge, Rafael Stelmach. Pulmonary Division, Heart Institute (InCor) - University of São Paulo Medical School, São Paulo, SP, Brazil

Persistent functional impairment in some severe asthmatics, even after maximal treatment, is usually linked to inflammation, which does not explain all asthma limitations and seems to be determined by small airways structural changes too.

Objective: Evaluate functional mechanisms related to persistent airflow obstruction (PAO) after an intensive therapeutic regimen in severe asthmatics.

Methods: Non-controlled severe asthmatics received high inhaled corticosteroid dose (ICs) plus LABA for 12 weeks and oral corticosteroid (OC) in the first two weeks, after which they were classified into PAO by an FEV₁ after BD < 80% plus FEV₁/FVC ≤ 0.70. Complete airway reversibility were labeled non persistent airflow obstruction (NPAO). Both groups were compared. Ex smokers >10 pack-years were excluded.

Results: At baseline, FEF₂₅₇₅, RV/TLC and resistance (Raw) were significant different between NPAO and PAO.

	NPAO (n=14)		PAO (n=48)	
	Baseline	After OC	Baseline	After OC
FEF 25-75	39±12	69±28*	24±13†	33±15*†
Raw	208±82	105±38*	330±119†	268±132†
VR/TLC	137±28	117±25*	173±32†	159±33*†
dN2	368±171	125±78*	572±336	338±296*†

All PAO values, including Slope of phase III of the single breath nitrogen washout test (dN2), became different after OC and did not return to normal. ACQ in NPAO decreased to near normal values (1.75±0.94).

Conclusion: Persistent obstruction phenotype in severe asthmatics showed a high heterogeneity of airflow measured by dN2 and early airway closure due to high RV/TLC suggesting a fixed impairment in small airways. VEF₁ changes in these patients seem to be influenced by small airway disease. PAO also impairs improvement in asthma control scores.

P2256

Change in pulmonary function abnormalities in sarcoidosis over time: A review of 75 cases

Christopher Atkins, Andrew Wilkes, Orion Twentyman, Chris Atkins, Chris Atkins. Department of Respiratory Medicine, Norfolk and Norwich University Hospital, Norwich, Norfolk, United Kingdom

Airflow obstruction is common on initial pulmonary function tests (PFTs) in Sarcoidosis. Little has been published about change in PFTs over time, or with treatment. We examined PFT change in patients diagnosed with Sarcoidosis over a 14 year period.

75 patients were included. Median follow-up was 5.1 years. Patients were divided into those treated prior to follow-up (n=39) and those not (n=36). Results are shown in table 1.

Treated patients tended to have greater deterioration of their PFTs. The difference was non-significant, except for a lower decline in FEV₁/FVC ratio in those untreated. Previous research (Miller et al. Chest 2011; 139:52-59) suggests fixed ratio values are less accurate than percentile predicted; here, there was no statistical difference in percentile change between groups.

Absolute FEV₁ and FVC values declined in both groups, though less in those untreated. Both groups showed greater than expected annual decline in FEV₁

Abstract P2256 – Table 1. Absolute and centile values (baseline, follow-up and within-group differences)

Outcome	Presentation		Follow-up		Within-group difference		Between-group mean difference (95% CI)
	Untreated	Treated	Untreated	Treated	Untreated	Treated	
FEV1 (L)	2.83	2.61	2.77	2.38	-0.07*	-0.23*	0.16* (-0.05-0.37)
FVC (L)	3.66	3.40	3.65	3.31	-0.01*	-0.09*	0.08* (-0.17-0.34)
FEV1/FVC Ratio	77.4%	77.2%	76.2%	72.1%	-1.2%	-5.2%	4% (0.58-7.42)
FEV1 (centile)	35.5	25.5	50.9	38.3	15.5	13.0	2.64 (-8.56-13.85)
FVC (centile)	46.1	32.7	68.8	58.8	22.7	26.3	-3.39 (-17.28-10.50)
Ratio (centile)	34.4	35.7	34.7	28.5	0.3	-6.5	7.47 (-4.90-19.385)

*L/year change.

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(Kerstjens et al. Thorax 1997;52:820-7), though both improved their percentile predicted values, with no significant difference in FEV1 or FVC change between groups.

P2257**Lung clearance index is a reliable and sensitive measure of airways disease in bronchiectasis**

Stephen Rowan¹, Judy Bradley², Madeleine Ennis¹, Alex Horsley³, Nicholas Bell⁴, Per Gustafsson⁵, Joseph Stuart Elborn¹. ¹Centre for Infection and Immunity, Queen's University Belfast, United Kingdom; ²School of Health Sciences, University of Ulster, Belfast, United Kingdom; ³Wythenshawe Hospital Adult CF Centre, University Hospitals of South Manchester, Manchester, United Kingdom; ⁴Bristol Adult CF Centre, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom; ⁵Department of Pediatrics, Central Hospital, Skövde, Sweden

Introduction: In bronchiectasis (BE), there is a need for a sensitive outcome measure that is responsive to interventions, particularly in those with mild disease. FEV1 is insensitive to small airways disease and is often within normal range in BE. Lung clearance index (LCI) is a measure of ventilation inhomogeneity derived from multiple breath washout (MBW).

Objective: To assess intra and inter-visit repeatability of LCI and determine the relationship between FEV1 and LCI in stable BE.

Methods: Inclusion criteria: HRCT diagnosis of BE within 5 years; clinically stable (>4 weeks no infective symptoms); no features of CF. Participants attended for 2 visits, 2 weeks apart. At each visit they performed MBW in triplicate, using 0.2% SF6 and a modified InnocoTM device. LCI was derived from the mean of at least 2 acceptable washouts. Spirometry was performed to ATS/ERS standards.

Results: 30 patients (14M/16F) attended for 2 visits. The mean (SD) age was 56.6 (14) yrs. Mean (SD) FEV1% predicted was 84.8 (20.7), range (40-117). Mean (SD) LCI was 9.2(1.7) on visit 1 and 9.3(1.9) on visit 2 (normal <7.5). The intra-visit and inter-visit intraclass correlation coefficient was 0.94. LCI negatively correlated with FEV1 ($r=-0.73$, $p<0.001$) and FEF25-75 ($r=-0.84$, $p<0.001$). Sensitivity of LCI, FEV1 and FEF25-75 for the diagnosis of bronchiectasis by CT was 83%, 40% and 73% respectively.

Conclusions: This is the first report of LCI in BE. LCI has good intra and inter-visit repeatability. Across a range of FEV1 there is a strong relationship between LCI and FEV1. LCI is a more sensitive test of lung function than FEV1 and FEF25-75, and is abnormal in the majority of people with BE who have a normal FEV1.

P2258**Managing asthma in the outpatient clinic – Can the FEV1/FVC indicate when to do a reversibility test?**

Celeste Porsbjerg, Asger Sverrild, Lise Stensen, Birgitte Nybo Jensen, Backer Vibeke. Respiratory Research Unit, Bispebjerg Hospital, Copenhagen, Denmark

Background: Testing for reversibility to SABA often constitutes the first step of a diagnostic assessment of asthma. However, patients with a normal or near-normal lung function often do not have significant reversibility, and performing reversibility testing in these patients may not be cost-effective.

Aim: To describe the value of the FEV1/FVC ratio using lower limit of normal (LLN) for predicting significant reversibility to SABA, and to define optimum cut-points that might be applied clinically.

Methods: The MAPOut I study is a retrospective observational study of all patients consecutively referred to a tertiary hospital specialist clinic over a 12-month period, on suspicion of asthma (n=221).

Results: In total, 122 subjects (55%) had a reversibility test performed, among whom 28 (23%) had a significant response to beta-2-agonist, defined as an increase in FEV1 of 12% or more, and at least 200 mL. The area under the curve of the FEV1/FVC % of the LLN for predicting reversibility was 0.76 ($p<0.001$). The FEV1/FVC ratio was above the LLN in 77% of newly referred asthma patients, including subjects who had a reversibility test performed (94/122 (77%)). Only 14% of subjects with an FEV1/FVC above the LLN had significant reversibility, compared to 54% of subjects with an FEV1/FVC ratio below the LLN.

Conclusion: Absence of significant airflow obstruction at rest was associated with a low likelihood of reversibility to beta-2-agonist. The majority of subjects referred for specialist assessment on the suspicion of asthma did not have airflow obstruction. In these subjects, alternative diagnostic strategies may be more cost-effective.

P2259**The prediction of airway wall thickening by computer aided lung sound analysis**

Surussawadi Mackawan¹, Anne Bruton¹, Anna Barney², Michael Bennett³, Tom Havelock³. ¹Faculty of Health Sciences, University of Southampton, Hampshire, United Kingdom; ²Institute of Sound and Vibration Research, University of Southampton, Hampshire, United Kingdom; ³Southampton Centre for Biomedical Research, University Hospital Southampton NHS Foundation Trust, Southampton, Hampshire, United Kingdom

Computer Aided Lung Sound Analysis (CALSA) has been used to detect and

analyse added lung sounds to aid diagnosis of many respiratory diseases. The wall area of the main bronchi, expressed as a percentage of the cross-sectional area of each branch, is a biomarker of chronic airway inflammation which is raised in COPD. The objective of this study was to explore the possible relationship between characteristics of crackles measured by CALSA and percentage of wall area of the main bronchi measured by High Resolution Computed Tomography (HRCT), and hence the possibility of using crackles as a biomarker of COPD. 26 participants (9 healthy non-smokers, 9 healthy smokers and 8 COPD) were recruited. Lung sound data were recorded using a digital stethoscope. HRCT scans were conducted using a Siemens Sensation 64 CT scanner and the resulting data were analysed using the Pulmonary Workstation 2 (Vida Diagnostics, Iowa, US) software to give measurements of airway geometry. The results showed that the percentage of wall area at the right upper bronchus correlated with the two cycle duration of crackles ($r=-0.39$, $p=0.025$) recorded at the right upper lobe (RUL), the number of crackles per breathing cycle (NCpB) at RUL ($r=-0.49$, $p=0.005$) and NCpB at right lower lobe ($r=-0.49$, $p=0.006$). Additionally, the NCpB at RUL was found to significantly predict the percentage of wall area at the right upper bronchus (adjusted $R^2=0.20$, $R^2=0.24$, $p=0.010$). These initial results suggest NCpB might be useable to predict changes in percentage of wall area caused by the chronic inflammation of the main bronchi, though a larger sample is needed to confirm it. This suggests that crackles could possibly be used as a biomarker of COPD.