417. Screening, diagnosis, staging and treatment strategies for lung cancer

P4184

Validation of CALIPER (Computer-aided lung informatics for pathology evaluation and rating) for the non-invasive assessment of pulmonary nodules of the adenocarcinoma spectrum

Fabien Maldonado[1], Sushravya Raghunath[2], Marie Christine Aubry[3], Brian Bartholmai[6], Jennifer Boland Froemming[3], Mariza De Andrade[4], Ronald Karwoski[2], Srinivasan Rajagopalan[2], Richard Robb[2], Ping Yang[5], Eunhee Yi[3], Tobias Peikert[1]. *[1]Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, United States; [2]Department of Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN, United States; [3]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, United States; [4]Department of Biostatistics, Mayo Clinic, Rochester, MN, United States; [5]Department of Health Science Research, Mayo Clinic, Rochester, MN, United States; [6]Department of Diagnostic Radiology, Mayo Clinic, Rochester, MN, United States*

Rationale: The growing utilization of high-resolution computed tomography (HRCT) for clinical diagnosis and lung cancer screening results in identification of pulmonary nodules of unknown clinical significance. Non-invasive strategies

for the individualized management of these lesions are required. In a pilot study we have demonstrated the consistent classification of pulmonary nodules of the adenocarcinoma spectrum using CALIPER.
Methods: Two pumonary patholgists independently assessed histopathologic tissue invasion in 72 surgically resected pulmonary nodules (≤ 3cm) of adenocarcinoma spectrum from 68 patients. Based on consensus, all lesions were categorized as either NINV-"non-invasive" (≤5mm invasion), n=6 or INV-"invasive" (>5mm invasion), n=66. CALIPER mapped the individual HRCT voxels (pre-operative HRCT) within all the nodules to one of the previously identified 9 unique radiological patterns. The nodules were categorized as INV or NINV based on the relative distribution of the patterns. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for CALIPER-based detection of tissue invasion were calculated.
Results: Sensitivity, specificity, NPV and PPV were respectively 98.5%[90.7-99.9%], 66.7%[24.1-94%], 97%[88.7-99.4%] and 80%[30-98%]. Only one case was identified as NINV by CALIPER and as INV by the pulmonary pathologists.
Conclusion: CALIPER represents a promising tool for non-invasive risk stratification of pulmonary nodules of the adenocarcinoma spectrum. Further prospective and retrospective validation of our data is currently ongoing.

P4185
Probability of malignancy based on automatic segmentation and software measurements of nodules in the Danish lung cancer screening trial (DLCST)
Zaigham Saghir[1], Colin Jacobs[2,3], Bram van Ginneken[3], Marleen de Bruijne[4,6], Asger Dirksen[1], Jesper Holst Pedersen[5]. *[1]Department of Respiratory Medicine, Gentofte University Hospital, Hellerup, Denmark; [2]Fraunhofer MEVIS, Bremen, Germany; [3]Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [4]Department of Computer Science, University of Copenhagen, Denmark; [5]Department of Thoracic Surgery, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark; [6]Department of Medical Informatics and Radiology, Erasmus MC - University Medical Center, Rotterdam, Netherlands*

Introduction and aim: With the widespread use of chest CT in clinical and screening settings pulmonary nodules are detected more frequently than ever, and the risk of malignancy needs to be determined.
Materials and methods: In DLCST, 4,104 current and former smokers, with a history of at least 20 pack years and age between 50-70 years, were randomized to either five annual multi-slice low-dose CT screenings or no screening. All participants had an annual visit to the screening clinic where lung function tests and questionnaires concerning health, lifestyle, smoking habits and psychosocial consequences of screening were performed. All scans were double-read by two experienced chest radiologists and the location and size were registered. Nodules between diameters of 5-15 mm were considered indeterminate, and rescanned after three months. Participants with nodules larger than 15 mm were referred to diagnostic workup, as were those with growing nodules. Lung cancer was diagnosed by pathological evaluation.
Using volumetric software nodules were segmented automatically and for the solid and sub-solid components mass and volume were calculated as well as the largest axial diameter. All automated nodule-segmentations were visually reviewed for correctness and adjusted if needed.
Results and conclusion: We are currently analyzing the data by logistic regression with malignancy as outcome and nodule measurements and risk factors such as age, sex, smoking status and history and COPD-status as explanatory variables. The results will be presented at the ERS 2012 in Vienna.

P4186
Emphysema, COPD and lung cancer screening. Update of an ongoing study
Pablo Sanchez, Maria Sanchez-Carpintero, Juan Bertó, Pilar Rivera, Ana Belén Alcaide, Juan Pablo de Torres, Arantxa Campo, Jorge Zagaceta, Javier Zulueta. *Neurología, Clinica Universidad de Navarra, Pamplona, Spain*

Recently, screening with low-dose CT (LDCT) has been shown to reduce mortality from lung cancer. We reported that emphysema on a LDCT, but not COPD (FEV1/FVC<70%), is associated with an increased risk of lung cancer. We present an update of our screening study.
Data comes from a prospective cohort of an ongoing lung cancer screening study held at our center. From 2000 to 2011, current and former smokers of at least 40 years of age and at least 10 pack-years of smoking were recruited. All had annual LDCTs and most a baseline spirometry. Lung cancer incidence density and its association with risk factors were calculated with logistic regression.
From a cohort of 2697 subjects, 1925 (25% females) who had LDCTs and a spirometry were analyzed. Median age and smoking history were 55 and 33 pack-yrs, respectively. Emphysema on LDCT and airway obstruction on spirometry were found in 25% and 28%, respectively. Lung cancer was diagnosed in 38 subjects, 26 on the baseline LDCT and 12 in annual follow-ups. The most frequent hystologic types were adenocarcinoma (53%) and squamous cell carcinoma (21%). There were 4 (11%) small cell carcinomas (all in stages IIIB or IV). The majority of NSCLC were identified in stage I (79%). The incidence density for lung cancer in subjects with emphysema, COPD, or with none was 36.1, 24.7 and 2.5 per 1000 person-yrs, respectively. Adjusting for age, sex and smoking, emphysema (OR 4.76; IC95% 2.32-9.77) and airway obstruction (OR 2.65; IC 95% 1.26-5.57) were independent risk factors for lung cancer.
In a cohort of individuals participating in a lung cancer screening study, emphysema and airway obstruction are significantly associated with a greater risk of lung cancer.

P4187
Measurement of alveolar nitric oxide in patients with lung cancer
Anastasios Kallianos[1], Sotirios Tsimpoukis[2], Harpidou Andriani[2], Rapti Aggeliki[1], Syrigos Konstantinos[2]. *[1]2nd Pulmonary Clinic, Sotiria Hospital, Athens, Greece; [2]Oncology Unit, Sotiria Hospital, Athens, Greece*

Introduction: The presence of NO as a marker of airway inflammation and indirectly as a general indicator of inflammation and oxidative stress-incrimination as incriminating factor in lung cancer at an early stage and then the treatment of disease after chemotherapy.
Purpose: We studied whether exhaled NO levels altered by 3 cycles of chemotherapy the levels at diagnosis and whether directly or indirectly related to the course of disease. Also, correlation levels of NO with other markers of inflammation.
Method: We studied 28 patients early diagnosed -18 men and 10 women with lung cancer.We analyse.blood tests for control of inflammatory markers, functional pulmonary tests and alveolar exhaled nitric oxide.
Results: Recorded decrease in exhaled NO after 3 cycles of chemotherapy in all patients regardless of histological type and stage.
28 patients with a mean 6.8 NO occurs after 3 cycles average 4.9, a value which is normal.
Also appears strong correlation between NO before and after chemotherapy and CRP ($p < 0.05$, r 0.42 pre) and ($p < 0.045$, r 0.64 after).
It is a further breakdown of data by the statistical program SPSS, with subgroups for analysis based histological types.
Conclusions: NO alveolar as an indicator of airway inflammation, indicates response to chemotherapy in lung cancer. Also the inflammatory process in lung cancer confirmed and indicates response to chemotherapy through an index which is sensitive to inflammatory diseases of the airways and not reused in lung cancer before and after chemotherapy.

P4188
Risk assessment of venous thromboembolism in lung cancer – Utility of Khorana model
Carina Gaspar, Dalila Ferreira, Susana Simões, Paula Alves, Agostinho Costa. *Pneumology, Pulido Valente Hospital - Centro Hospitalar Lisboa Norte, Lisboa, Portugal*

Background: Venous thromboembolism (VTE) is a common and costly complication in patients with lung cancer. Research is focusing on identifying high-risk patients who might benefit from primary thromboprophylaxis. For this purpose, Khorana built a predictive model of VTE in cancer patients receiving chemotherapy as outpatients, including 5 independent risk factors: site of cancer, pre-chemotherapy platelet count, hemoglobin level or use of red cell grow factors, leukocyte count and body mass index.
Aim: To evaluate the utility of the Khorana model to predict VTE in lung cancer patients undergoing chemotherapy.
Methods: We conducted a retrospective study including all patients diagnosed with lung cancer between January and July/2011 who underwent chemotherapy as outpatients in Pulido Valente Hospital, in Lisbon. Risk for TVE according to Khorana model was calculated in patients with and without TVE.
Results: From 241 patients, 6 developed pulmonary embolism (2,5%), 12 deep venous thromboembolism (5,0%) and 2 had both (0,8%), for an overall rate of VTE of 8,3%. Adenocarcinoma, metastatic disease and history of cerebrovascular disease were significantly ($p<0.05$) more common in the group of patients with TVE. Using Khorana model, 35,0% of patients were at high risk for VTE in the group of patients with TVE, compared to 14,3% in the group without (p=0,016).
Conclusion: In our experience the Khorana model proved to be useful in predicting TVE in a cohort of lung patients receiving chemotherapy. The development of risk-assessment models of TVE for lung cancer that integrate other risk factors specific for this type of cancer should although be encouraged.

P4189
Arterial thromboembolic complications in patients with lung cancer – Impact on survival
Catharina Crolow[1], Markus Samulowski[1], Timo Weiss[1], Torsten Blum[1], Jens Kollmeier[1], Nicolas Schönfeld[1], Wolfram Grüning[2], Torsten T. Bauer[1]. *[1]Department of Pneumology, Lungenklinik Heckeshorn, HELIOS Klinikum Emil von Behring, Berlin, Germany; [2]Department of Pneumology, HELIOS Kliniken Schwerin, Germany*

Background: Venous thromboembolic events (TEE) are a frequent complication in patients with lung cancer (LC) (own data: total 7.6%). Yet the impact of arterial TEE on the patient's prognosis and preventive treatment strategies is unclear.
Aim: To evaluate the frequency of arterial TEE and their prognostic relevance in LC.
Methods: In this monocentric, observational study all patients with primary diagnosis of LC between Jan. 2008 and Dec. 2010 were prospectively recorded and retrospectively evaluated with regard to arterial TEE.

Results: Within 36 months 1940 patients (1209 men, 731 women) were diagnosed with LC (SCLC 10.3%, NSCLC 89.7%). Arterial TEE were documented in 51 patients (2.6%) with ischemic stroke as leading event (n=23, 1.2%), followed by events located in coronary (n=14, 0.7%), peripheral (n=12, 0.6%), mesenterial (n=4, 0.2%) and extracranial arteries (n=3, 0.6%). Kaplan-Meier-survival analysis showed shorter survival (p=0.003) for the group of patients with an arterial TEE (median survival 283 days vs. 479 days).

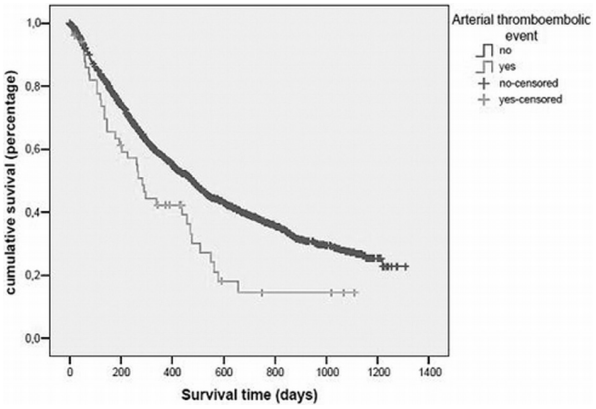


Figure 1. Kaplan-Meier survival analysis.

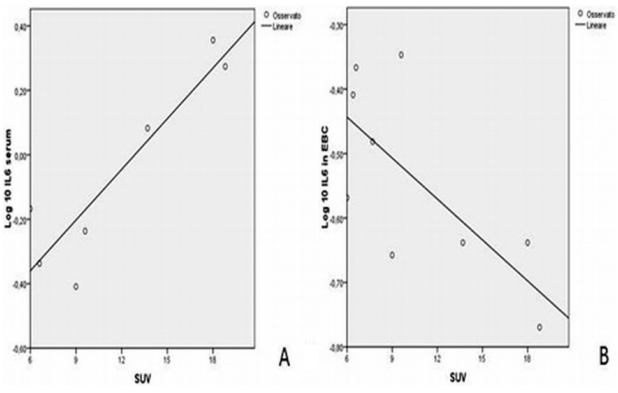
Conclusion: Besides an increased risk for deep venous TEE the frequency of arterial TEE in patients with LC is also increased. The tumor itself, chemotherapy and frequent cardiovascular comorbidities are believed to increase this risk and result in a significant worse prognosis. These data support prospective studies on primary antithrombotic prophylaxis in patients with LC.

P4190

Correlatin between PET scan and cytokine in non-small cell lung cancer (NSCLC)

Beatrice Culla[1], Pierluigi Filosso[3], Marta Morando[2], Caterina Bucca[4], Giovanni Rolla[2], Riccardo Cristofori[3], Marta Malandra[2], Arianna Vaudano[4], Monica Boita[2], Luisa Brussino[2]. *[1]Medical and Surgical Disciplines, University of Turin, Italy; [2]Biomedical Science and Human Oncology, University of Turin, Italy; [3]Thoracic Surgery, University of Turin, Italy; [4]Clinical Phathophysiology, University of Turin, Italy*

Background: Systemic and local inflammatory microenvironment may be an important contributor to morbidity and mortality associated with NSCLC. Exhaled breath condensate(EBC) is a non-invasive method to collect airway lining fluid for assessing lung inflammation. Interleukin-6 (IL-6) is associated with poor prognosis and correlates with neoplastic cachexia and with stage of disease. PET scan has been included in standard staging workup and the standardized uptake value(SUV) of PET-scan has been shown to correlate with poor prognosis in lung cancer.
Aim and Objective: To assess the correlations between serum and EBC IL-6 levels and SUV in patients with NSCLC.
Methods: Fifteen consecutive patients (12 males, mean age 64 years, range 39-82) receiving a curative resection for NSCLC were enrolled. All the patients underwent PET scan and IL-6 values measurement both in serum and EBC.
Results: PET scan was positive in all the patients with a mean SUV value 10.64±4.28(range: 6-18.8). Mean IL-6 value was 1.05 pg/ml ± 1.27 in serum and 0.29 pg/ml ± 0.09 in EBC. Significant correlation between SUV and IL-6 levels both in serum and in EBC was found (r= p<0.001 and r = p<0.05 respectively)



Conclusions: The observed relationship suggest that lung and systemic inflammation is proportional to tumor metabolic activity.

P4191

High performance and timely care of integrated FDG-PET and diagnostic CT in a rapid outpatient diagnostic program for suspected lung cancer patients

Pepijn Brocken[1], Hendrikus Van der Heijden[1], Richard Dekhuizen[1], Liesbeth Peters-Bax[2], Lioe-Fee De Geus-Oei[3]. *[1]Pulmonary Diseases, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [2]Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [3]Nuclear Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands*

Introduction: The objective of this study was to evaluate the diagnostic performance of ^{18}F-fluorodeoxy-glucose-Positron Emission Tomography with integrated contrast enhanced Computed Tomography (FDG-PET/CT) as a routine diagnostic tool in a Rapid Outpatient Diagnostic Program (RODP) for patients referred on the basis of a chest X-ray suspicious of lung cancer.
Methods: A retrospective chart study was conducted of all patients referred to the two-day RODP of our tertiary care university clinic between 1999 and 2009 after an abnormal chest X-ray. We analyzed timeliness of care and the diagnostic performance of FDG-PET/CT to differentiate between malignant and benign lesions.
Results: In 386 patients available for analysis, 260 patients were diagnosed with non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC) of both subtypes; 23 patients had another type of malignancy, 78 patients had certain benign disease, and in 45 patients the diagnosis was not pathologically confirmed but a median 24.5 months follow up confirmed a benign outcome. Sensitivity, specificity, negative predictive value, positive predictive value and accuracy of FDG-PET/CT to differentiate lung cancer from benign disease were 97.7%, 60.2%, 92.5%, 84.0% and 85.7% respectively. For lung cancer patients, median referral time was seven days, diagnostic delay was 2 days and therapeutic delay 19 days.
Conclusion: FDG-PET/CT in an RODP setting for suspected lung cancer has high performance in detecting cancer and facilitates timely care.

P4192

A proposal in small cell lung cancer staging according to TNM system

Kostas Zarogoulidis[1], Dimitris Latsioe[1], Kostas Porpodis[1], Paul Zarogoulidis[1], Nick Antoniou[1], Ellada Elephteriadou[1], Efimia Boutsikou[1], Theodore Kontakiotis[1], Jan-Paul Sculier[2]. *[1]Pulmonary, Aristotle University, Thessaloniki, Greece; [2]Oncologie thoracique, Institut Jules Bordet, Bruxelles, Belgium*

Background: Many pts with limited disease [LD] behave similarly to those with extensive disease [ED] from the prognostic point of view. On the other hand, a proportion of pts with ED SCLC behave similarly to those with LD. Moreover, the 7th (IASLC) TNM classification has not been evaluated with recent, large scale studies in SCLC.
Patients and methods: In this retrospective analysis 764 pts with proven SCLC were included managed with the same therapeutic protocols based on platinum analogues. Of these pts, 278 (36.4%) had LD, while 486 (63.6%) had ED. This classification was based on the following investigations: chest radiography, computed tomography of chest, abdomen and brain, fiberoptic bronchoscopy, isotope bone scan, sputum cytology and haemotological and biochemical profile. We also grouped the pts according to new TNM classification (seventh edition).
Results: A statistically significant difference was found in survival among the LD SCLC pts with (IA + IB), (IIA + IIB + IIIA) and IIIB stage (p<0.001). Similarly, we found a statistically significant difference in survival in ED SCLC pts with (IIA + IIB + IIIA), IIIB and IV stage (p<0.001).

Table 1. Survival according to the stage of the disease

Disease Stage	Number of patients	Median survival (days)	95% CI
Stage IA + IB	40	512	419.029–604.971
Stage IIA + IIB + IIIA	211	348	296.630–399.370
Stage IIIB	136	277	214.959–339.041
Stage IV	377	236	220.387–251.613
Total	764	286	270.474–301.526

Conclusions: A new classification of SCLC can be proposed which includes four stages based on TNM classification of NSCLC. [(Stage IA+IB), (Stage IIA+IIB+IIIA), (Stage IIIB) and (Stage IV)].

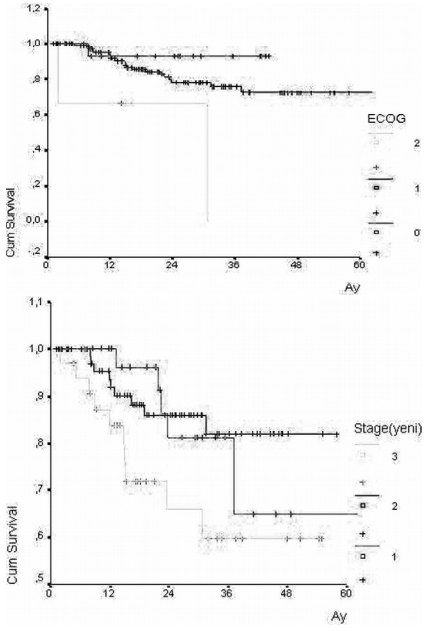
P4193

The prognostic impact of stage and performance status on surgically resected non-small cell lung cancer

Mesut Bayraktaroglu, Engin Aynaci, Pinar Yildiz. *Pulmonology, Third Clinic, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey*

In our study, pathological stage and Eastern Cooperative Oncology Group (ECOG) performance status were assessed in surgically resected non-small cell lung cancer (NSCLC) patients. The aim was to determine the effects of tumor stage and performance status on overall survival and disease-free survival in our cases.
Methods: 148 consecutive patients (mean age 57.9±8.29 years, min 36 max 76) were included in this study. 12 (%8.1) patients were women and 136 (%91.9) were men. Each patient was staged according to the TNM classification.

Results: ECOG performance status was related with both mean survival and disease-free survival time (respectively p=0.011 and p=0.044). 148 patients were grouped by using 1997 TNM and 2009 IASLC staging systems. According to survival analysis, disease-free survival was not related with stage but mean survival analysis revealed that stage 3 cases had significantly worse survival compared to stage 1 cases (p=0.005).



Conclusion: According to our results, survival was significantly worse in stage 3 patients and patients with poor performance status.

P4194

The role of pequi fruit (Caryocar brasiliense Camb) pulp oil, as a natural source of antioxidants, in experimental lung cancer

Natália Beatriz Rigoldi Colombo[1], Edwin Roger Parra[1], César Koppe Grisólia[2], Márcia Hage[4], Denise Frediani Barbeiro[5], Vera Luíza Capelozzi[1]. [1]*Pathology, Faculdade de Medicina da Universidade de São Paulo, Brazil;* [2]*Genetic and Morphology, Universidade de Brasília, Brasilia, Brazil;* [3]*Laboratory of Experimental Atmospheric Pollution, Faculdade de Medicina da Universidade de São Paulo, Brazil;* [4]*Clinical Emergency, Faculdade de Medicina da Universidade de São Paulo (FMUSP), Brazil*

Background: Caryocar brasiliense Camb, most known as pequi, is a Brazilian fruit that has high levels of antioxidants properties. The aim of this study was to evaluate the antioxidant activity of the pequi oil.
Methods: 18 male BALB/c mice was studied: 14 animals received by gavage 0,5μL/mg/day of pequi oil (Control + CBCoil = 4) during 75 days. After 15 days, 10 mices received two doses of 1,5g/kg intraperitoneal of urethane (Urethane + CBC oil = 10). The other 4 animals were only submitted to the two doses of urethane (Urethane group = 4). After 75 days, these groups were sacrificed. Antioxidant activity of pequi oil was evaluated in the lung tissues by the biochemical TBARS test (Thiobarbituric acid-reactive substances) and DNA damage by the comet test method.
Results: The lung parenchyma from the Urethane groups without oil and with oil showed neoplasic formations induced by the chemical carcinogenesis in contrast with Control + CBC oil group.The image analysis of the comet assay showed a statistical significant decreased of the DNA damage cells in the Urethane + CBC oil group when compared with urethane group. TBARS test showed a significant decreased of the lipid peroxidation in the Urethane + CBC oil, similar as values of the Control + CBC oil, when compared with Urethane group.
Conclusion: We conclude that the different natural antioxidant components found in the pequi oil are efficient to diminish the oxidative stress status and the DNA damage in chemical carcinogenesis induced by urethane experimental lung cancer, suggesting that this type of strategies may have a greater impact in lung cancer treatment.
Financial Support: FAPESP, CNPq.

P4195

Evaluation of outpatient infections in lung cancer patients treated with chemotherapy and/or radiotherapy

Vasileios Kouranos[1], Emily Tsaroucha[1], Antonis Vassias[2], John Arapis[1], John Gkiozos[2], Konstantinos Syrigos[2]. [1]*8th Pulmonary Clinic, General Hospital of Chest Diseases "Sotiria", Athens, Greece;* [2]*3rd Oncology Unit, University of Athens, Greece*

Introduction: Infections are important causes of morbidity and mortality in lung cancer patients. The myelotoxicity caused by the administration of either the chemotherapeutic regimens or the radiotherapy increases the risk of potentially life-threatening infection.
Methods: This prospective study included all patients with lung cancer who referred with signs or symptoms of infection between September 2009 and October 2011. Data concerning patient's history, disease's diagnosis, management and therapy and infection's signs, symptoms and documentation were collected.
Results: Seventy one patients with lung cancer were enrolled with febrile episodes and/or microbiologically or otherwise documented infection. Forty six patients (64.8%) presented with non-small cell lung carcinoma, while 22/71 patients (31%) and 3/71 patients (4.2%) had small cell lung cancer and mesothelioma respectively. Fifteen patients (21.1%) presented with FN and totally 43/71 (60.6%) patients required hospitalization for parenteral therapy upon admission. The predominant site of the infections was the lung in 59/71 patients (83.1%). In the hospitalized setting 3 episodes of bacteremia with Staphylococcus aureus were reported and microbiologically documented infections accounted for 26.7% of the hospitalized patients. The overall mortality rate was 9.8%, while only 1 patient died in the outpatient setting despite the antibiotic therapy.
Conclusion: This study showed that the early detection and control of infection in lung cancer patients receiving therapy may improve their survival. Recognition of predisposing factors for infections and possible therapy toxicities should be evaluated carefully.

P4196

Evaluation of quality of life in patients with primary and metastatic lung cancer following radiofrequency ablation

Julia Beeson, Sunny Kaul, Winston Banya, Paras Dalal. *Thoracic Radiology, Royal Brompton & Harefield NHS Foundation Trust, London, United Kingdom*

Objective: Radiofrequency ablation (RFA) is an increasingly utilised treatment option for high risk patients with primary lung cancer and metastatic lung disease. We assessed quality of life in patients undergoing RFA for primary and secondary lung cancers at this institution in patients deemed unfit for surgical intervention.
Materials and methods: 55 patients, (42 primary lung cancer and 13 metastatic lung tumours) were entered into the study. One standard instrument was used to measure quality of life, the European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30). An integrated system for assessing health-related quality of life of cancer patients. All procedures were performed by a single operator. All patients were clinically and radiologically followed-up in a standardised way, all questionnaires were collected by a single associate pre treatment and one year post ablation. Data was analysed using the Stata version 10 software.
Results: The EORTC scores were converted to physical function, respiratory function, emotional functioning and global health scales, mean value for each scale was calculated pre and post ablation. There was a reported improvement in all four scales after ablation. The paired t test was used to assess statistical significance of the results. This revealed statistically significant improvement in emotional function (p =0.023) and the global health scales (p = 0.008).
Conclusion: This retrospective study demonstrates that patients undergoing ablation therapy for primary and secondary lung cancer describe overall improved function with statistically significant improvement in emotional and global health scales.

P4197

Is surgical resection of M1a lung adenocarcinoma with metastatic pleural nodules really a useless choice?

Jinkyeong Park[1], Mi-Ae Kim[2], ChangMin Choi[2], HyungRyul Kim[3]. [1]*Pulmonary and Critical Care Medicine, Wongwang Univ. Sanbon Hospital, Gunpo, Gyeonggi, Korea;* [2]*Pulmonary and Critical Care Medicine, Asan Medical Center, Univ. of Ulsan College of Medicine, Seoul, Korea;* [3]*Thoracic and Cardiovascular Surgery, Asan Medical Center, Univ. of Ulsan College of Medicine, Seoul, Korea*

According to a revised 7th TNM classification of NSCLC, malignant pleural nodules are defined as a M1a stage. This study attempts to validate an effect of the surgical resection of a primary lung lesion to the survival of lung adenocarcinoma with metastatic pleural nodules which was not detected on chest CT and PET scan. From 1995 to 2010, we retrospectively investigated in 36 patients who had adenocarcinoma with metastatic pleural nodules. There were no evidences of pleural nodules on chest CT or PET/CT before surgery. Whenever unexpectedly pleural nodules were at surgery, additional surgical resection of the nodules were decided by surgeon. 36 patients of adenocarcinoma were upstaged to M1a because malignant pleural nodules found at operation. 22 patients had only "open and closure" exploratory thoracotomy (Non-Surgery group) and 14 patients had surgical resection of a primary lung adenocarcinoma (Surgery group). There were no significant differences of age and FEV1 (%) between Surgery group and Non-Surgery group. The 1-year survival rate of the total 36 patients was 92% (Non-surgery group (86%) vs. Surgery group (100%),p=0.157). The 2-year survival rate was 75% (Non-surgery group (66%) vs. Surgery group (89%), p=0.123). The 5-year survival rate was 26% (Non-surgery group (12%) vs. Surgery group (74%),p=0.011*). The median time to progression of the total 36 patients was 14.6±3.7months (Non-surgery group 4.6±1.0months vs. Surgery group 39.5±12.7months). Surgical resection of primary lung cancer would prolong the time to progression and improve the 5-year survival rate in some adenocarcinoma patients with invisible metastatic pleural nodules.

P4198

Determinants of relapse and survival in completely ressected non small cell lung cancer

Filipa Soares Pires[1], Gabriela Fernandes[1,2], Ana Paula Vaz[1], António Morais[1,2], Conceição Souto Moura[2,3], Pedro Bastos[2,4], Venceslau Hespanhol[1,2].
[1]Pulmonology Department, Centro Hospitalar de São João, Pólo do Porto, Porto, Portugal; [2]Faculty of Medicine, University of Porto, Portugal; [3]Pathology Department, Centro Hospitalar de São João, Pólo do Porto, Porto, Portugal; [4]Thoracic Surgery Department, Centro Hospitalar de São João, Pólo do Porto, Porto, Portugal

Introduction: Lung ressection is the treatment of choice in Non-Small Cell Lung Cancer (NSCLC). Besides TNM staging, other features have been reported as significant prognostic factors.
Aim: To analyze factors affecting relapse and survival in NSCLC after complete ressection.
Methods: A retrospective study was conducted, including patients with NSCLC completely ressected in the last 12 years. Clinical and histological factors were assessed and its influence on survival free of relapse and overall survival was determined.
Results: 160 patients were included, 77.5% male and 22.5% female, with a median age of 65years. Relapse occurred in 69 patients (median survival free of relapse - 56 months). At univariate analysis, an association was found between reduced survival free of relapse and age≤62 years, clinical tumor size≥4cm, clinical TNM stage>IB, clinical T>1, clinical N>0, pathological TNM stage>IB, pathological T>2, pathological N>0 and vascular invasion. At multivariate analysis, tumor size≥4cm (p=0.004), pathological TNM stage>IB (p=0.023) and vascular invasion (p=0.024) were associated to a reduced survival free of relapse.
64 patients died (median overall survival – 112 months). At univariate analysis, an association was found between reduced overall survival and age≤62 years, clinical tumor size≥4cm, clinical TNM stage>IB, clinical N>0, pathological TNM stage>IB, pathological T>2, pathological N>0, vascular invasion and poor differentiation of tumor. At multivariate analysis, only pathological TNM stage>IB (p=0.029) remained associated a poorer overall survival.
Conclusion: Besides TNM staging, other features are important on relapse and survival and should be considered for adjuvant therapy.

P4199

Therapeutic options for operated adenocarcinoma patients in stages I or II

Anastasios Palamidas[1], Sophia - Antiopi Gennimata[1], Fotis Vlastos[1], Nikolaos Koulouris[1], Jean-Michel Vigneaud[2], Nadine Martinet[3]. *[1]First University Respiratory Clinic, Sotiria Chest Diseases Hospital, Athens, Greece; [2]d'Anatomie Pathologique, Hopital Central de Nancy, Nancy, France; [3]Laboratoire de Chimie, Laboratoire de Chimie des Molécules Bioactives, Nice, France*

Surgery is the only radical option for NSCLC therapeutic management. We studied the survival rates of operated NSCLC patients followed in the context of the ISO certified Nancy lung cancer biobank. During a period of 20 years, 26 patients (age = 59±9 years, p.yrs = 38±25, survival months = 30±15) were reoperated upon for curative purposes. The survival rates of these patients were compared to those of a matched control group of 26 NSCLC patients (age = 61±7 years, p.yrs = 45±26, survival months = 31±16) operated upon only once and no statistical significant difference was detected. Both groups received post-operation chemo-radiotherapy during the course of their disease. We also studied the survival rates of the most prevalent histotypes of these groups of NSCLC patients such as adenocarcinoma and squamous cell carcinoma. For patients with squamous cell carcinoma group, there was no statistical difference in survival between reoperated and once-operated patients in all stages. Nevertheless, for adenocarcinoma patients there was statistical significant difference in survival rates of 12 months favoring the reoperated patients in stages I – II (p = 0.0048). No statistical difference was presented between the lung adenocarcinoma groups in stages III – IV. We concluded that reoperation should remain an option for previously operated adenocarcinoma patients who are presented in stages I or II as their survival is expected to be longer in comparison to those who receive only post-operation chemo-radiotherapy.

P4200

Effect of statin therapy in patients with lung cancer on mortality, incidence of infections and pulmonary embolism

Stefan Krüger, Annika Vehl, Angelika Haselhuhn, Dirk Frechen. *Medical Clinic I, University Clinic RWTH, Aachen, Germany*

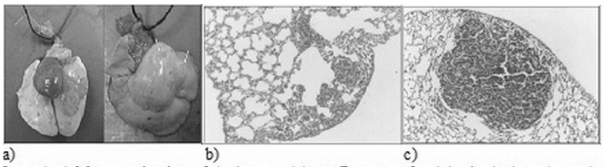
Background: Statins (S) have antiproliferative effects. Aim of this study was to assess whether S users with lung cancer (LC) had reduced risk of mortality, infections and pulmonary embolism.
Methods: We studied the association of S use in a retrospective study in 465 pts with first diagnosis of LC. The primary variables were stage and type of LC and S use at time of LC diagnosis and thereafter. During follow-up occurrence of death, infections and pulmonary embolism were recorded.
Results: 91 pts (19.6%) had S, 371 pts not. LC stages were I-IIIA 201 pts (43.2%), IIIb-IV 264 pts (56.8%). Pts with S were older (67.8±7.6 vs. 64.5±9.8 y., p < 0.005), had higher BMI, more often diabetes, myocardial infarction and chronic heart failure. Charlson comorbidity index was not different (5.2±2.2 vs. 5.7±2.4, p = 0.08). During follow-up 43% of the pts died. In Kaplan Meier analysis stage I-IIIA pts with S had lower survival compared with pts without S (log rank test, p<0.0001). However there was no significant difference in pts stage IIIb-IV. In pts < 65 y. survival was longer in pts with vs. without S (1002 (95%CI 588-3977) vs. 604 (95%CI 513-806) days, p<0.05). In pts ≥ 65 y. there was no difference in survival (493 (95%CI 308-776) vs. 693 (95%CI 555-917) days, p=n.s.). Incidence of severe infections and pulmonary embolism were not different in pts with and without S.
Conclusions: Long-term S therapy seems to reduce mortality in younger LC pts < 65 y., but not in pts ≥ 65 y. In stage I-IIIA pts S are associated with worse survival, whereas there is no difference in stage IIIb-IV pts. S do not reduce the incidence of severe infections and pulmonary embolism at follow-up.

P4201

Anaerobic exercise decreases the progression of lung cancer in experimental mice

Renato Paceli[1], Rodrigo Cal[2], Carlos Santos[4], Anna Morais[1], Cassiano Neiva[5], Antonio Cordeiro[3], Kazuo Nagamine[3,4], Patricia Cury[2]. *[1]Division de Pneumology, Heart Institute (InCor) School of Medicine, University of São Paulo, SP, Brazil; [2]Pathology and Forensic Medicine, School of Medicine of São José do Rio Preto – FAMERP, São Jose do Rio Preto, SP, Brazil; [3]Department of Epidemiology and Public Health, School of Medicine of São José do Rio Preto – FAMERP, São Jose do Rio Preto, SP, Brazil; [4]Physical Activity and Health Laboratory (LAFIS), School of Medicine of São José do Rio Preto – FAMERP, Bauru, SP, Brazil; [5]Laboratory of Metabolism and Physiology of Stress - mefE, Paulista State University -School of Science of Bauru – (Unesp), Bauru, SP, Brazil*

Introduction: Lung cancer is one of the most incident neoplasms in the world representing the main cause of mortality for cancer. Studies have suggested evaluate the effectiveness of the use of the physical activity in the suppression, remission and reduction of the recurrence of tumors.
Objective: To evaluate the effects of aerobic and anaerobic physical activity in the development and the progression of lung cancer.
Material and methods: Lung tumors were induced with a dose of 3mg of Urethane/kg, in 67 male Balb - C type mice, divided in three groups: Group 1 - 24 mice treated with Urethane and without physical activity; Group 2 - 25 mice with Urethane and subjected to aerobic swimming free exercise; Group 3 - 18 mice with urethane, subjected to anaerobic swimming exercise with gradual loading 5 to 20% of body weight. All the animals were sacrificed after 20 weeks.
Results: The median number of lesions (nodules and hyperplasia) was 3.0 for group 1, 2.0 for group 2 and 1.5 to 3 (p = 0.052). When compared only the presence or absence of lesion, there was a decrease in the number of lesions in group 3 compared with group 1 (p = 0.03) but not in relation to group 2. There were no metastases or other changes in other organs.



Legend: a) Macroscopic view of the lungs and heart. Presence of nodules in the lung (arrows); b) Microscopic view of the lung: hyperplasia (HE, 100X); c) Microscopic view of the lung: nodule (HE, 100X).

Conclusions: In this study, the anaerobic physical activity but not aerobic, diminish the incidence of experimental lung tumors.

P4202

Splenectomy inhibits tumor development and metastases in murine lung cancer models

Liran Levy[1], Inbal Mishalian[1], Zolotarob Lida[1], Rachel Bayuh[1], Zvi G. Fridlender[1,2]. *[1]Institute of Pulmonary Medicine, Hadassah-Hebrew University Medical Center, Jerusalem, Israel; [2]Department of Medicine, University of Pennsylvania, Philadelphia, PA, United States*

Introduction & Aims: It has been shown that inhibitors of the immune system (e.g. myeloid derived suppressor cells) reside in the spleen and inhibit the endogenous anti-tumor effects of the immune system. We hypothesized that excision of the spleen (splenectomy) can inhibit growth of relatively big tumors, and reduce metastases by modulating systemic inhibition of the immune system. Our long-term goal is to implement mechanisms elucidated in these studies into future clinical trials.
Methods: The clinical effect of splenectomy was evaluated in several murine lung cancer models. We compared immunological properties of blood and tumor after splenectomy or sham operation in tumor-bearing mice, using FACS analysis, RT-PCR and specific depletion studies.
Results: We found that splenectomy reduces tumor growth, can induce their regression, and decreases metastases. These effects disappeared in NOD/SCID mice. No significant changes in cell types were found in the blood. Splenectomy increased the percentage out of total tumor cells of neutrophils (2.4% vs. 4.9%, p=0.012), and macrophages (10.9% vs. 14.4%, p=0.014), which tended

to be less immune-inhibitory (non-M2/M2 macrophages ratio increased from 3.4 to 12.1, p=0.04). We further noted a tendency to increased activation of $CD8^+$ CTL (19.2% vs. 30%, p=0.09). Tumor microenvironment was found to be more pro-inflammatory following splenectomy (e.g. upregulation of MIG, TNF-α and IFN-γ). Using specific depletion of cells we evaluated the role of each cell in the effect of splenectomy.
Conclusions: Splenectomy inhibits the development of tumors and metastases in murine models of lung cancer, by changing the amount and characteristics of myeloid cells.

P4203
Direct medical costs of lung cancer in Oran hospital
Abdelmajid Snouber[1], Malika Metahri[1], Abdellatif Bennani[1], Souad Kebbati[1], Saada Chougrani[2], Malika Guermaz[1]. *[1]Chest Clinic, Faculty of Medicine, Oran, Algeria; [2]Epidemiologic Department, Faculty of Medicine, Oran, Algeria*

Objective: To analyse epidemiological profile of lung cancer and to evaluate expenses inherent in its diagnostic and therapeutic management.
Methods: Retrospective study of all cases of lung cancer notified during the period 2004-2008 in our chest clinic. Data concerning epidemiological characters and expenses which take into account, hospitalisation,diagnostic tests and treatment, were kept in an Epi-Info software package (Epi-info, version 6.0).
Results: Among 130 cases, 127 were studied. The mean age of our population was 66 years, age more than 50 years represented 80% of cases, 66,7% were male and 33,3% were female. Tobacco smoking concerned 91% of our patients.Thoracic pain respresented 20,6% of cases and cough 13% of cases. Frequent localisation of lung cancer was right upper lobar 68% and tumoral extension represented 80% of cases.Histological predominant lung cancer was epidermoide carcinoma with 35% of case followed by adenocarcinoma with 15% of cases. Global cost of hospitalisation was of £157086,86 with a mean cost per patient of £1208,36. Global cost of diagnostic tests was of £13350,71 with a mean cost per patient of £102,69 and global cost of of treatment was of £88395,17 with a mean cost per patient of £679,95.
Conclusion: Lung cancer management in hospital level remain problematic taken into account tobacco smoking threat and the higher expenses inherent in hospitalisation, diagnosis and treatment of the disease. The interest of a national plan against lung cancer is necessary to improve its management and to rationalize expenses.

Table 1.- Characteristics of study subjects

	Control(n=69)	COPD(n=63)	LC(n=63)
Age (year)*	49.3 (9.5)	74.3(10.0)	66.5(11.1)
Male/female	(42/47)	(57/3)	(60/17)
Smoker/ex-smoker/non smoker	20/24/35	34/1/1	50/22/9
Tabacco (packs-year)*			
Smokers	30.9(18.4)	123(29.5)	77.5(50.6)
Ex Smokers	26.5(21.6)	72.5(34.3)	63.6(34.1)
Histology (%)			
Squamous Cells			27.2%
Adenocarcinoma			39.5%
Undifferentiated			18.5%
Large Cells			2.5%
Carcinoid			1.2%
Small cells			11.1%
TNM (IA/IB/IIA/IIB /IIIA/IIIB/IV)			8.6%/6.2%/7.4%/2.5%/ 28.4%/14.9%/22.1%
GOLD (I/2/3/4) (%)		10%/32.5%/25 %/ 32.5%	13.6%/25.9%/13.6%/37.3% 29.6% without COPD

* Years (SD)

Table 2.- Frecuency. Comparation of biomarkers between different study groups.. p* values

	LC vs. Control	LC vs. COPD	LC with COPD vs. COPD
Hexanal	0.276	0.698	0.668
Heptanal	0.308	0.851	**0.051**
Octanal	0.769	0.759	0.710
Nonanal	0.454	0.645	0.807
Propanoic Acid	0.534	0.533	0.802
Nonanoic Acid	**0.011**	**0.001**	**0.001**

* Wilcoxon-Mann-Whitney

Table 3: Relationship between VOC in LC vs control group and COPD group.

	LC Group vs. Control Group			LC Group vs. COPD Group		
	Control	LC	p*	COPD	LC	p*
Hexanal	1.00	1.03 (0.46-2.68)	0.941	1.00	0.43(0.18-1.04)	0.062
Heptanal	1.00	1.42(0.79-2.29)	0.274	1.00	0.88(0.41-1.91)	0.752
Octanal	1.00	0.92(0.39-2.19)	0.848	1.00	1.10(0.36-3.41)	0.869
Nonanal	1.00	1.57(0.85-2.92)	0.152	1.00	1.08(0.0-2.32)	0.839
Propanoic Acid	1.00	1.24(0.68-2.28)	0.484	1.00	1.08(0.50-2.32)	0.853
Nonanoic Acid	1.00	2.53(1.21-5.29)	**0.014**	1.00	8.99(2.01-40.1)	**0.004**

*Odds ratio and 95% confidence interval based in logistic regression.