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Abstracts' Service

Ten-Year Survival in Patients with Idiopathic Pulmonary Fibrosis After Lung Transplantation

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Introduction. Idiopathic pulmonary fibrosis (IPF) is a progressive and lethal fibrosing lung disease with a median survival of approximately 3 years after diagnosis. The only medical option to improve survival in IPF is lung transplantation (LTX). The purpose of this study was to evaluate trajectory data of IPF patients listed for LTX and to investigate the survival after LTX.
Methods and Results. Data were retrospectively collected from September 1989 until July 2011 of all IPF patients registered for LTX in the Netherlands. Patients were included after revision of the diagnosis based on the criteria set by the ATS/ERS/JRS/ALAT. Trajectory data, clinical data at time of screening, and donor data were collected. In total, 98 IPF patients were listed for LTX. During the waiting list period, 30% of the patients died. Mean pulmonary artery pressure, 6-min walking distance, and the use of supplemental oxygen were significant predictors of mortality on the waiting list. Fifty-two patients received LTX with a median overall survival after transplantation of 10 years.
Conclusions. This study demonstrated a 10-year survival time after LTX in IPF. Furthermore, our study demonstrated a significantly better survival after bilateral LTX in IPF compared to single LTX although bilateral LTX patients were significantly younger.

Endosonography for Lung Cancer Staging: Predictors for False-negative Outcomes

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Objectives. Non-small cell lung cancer (NSCLC) guidelines recommend endosonography (endobronchial [EBUS] and/or transesophageal ultrasound [EUS]) as the initial step for mediastinal tissue staging. Identifying predictors for false negative results could help establish which patients should undergo confirmatory surgical staging.
Materials and methods. 775 NSCLC patients staged negative by EBUS, EUS or combined EUS/EBUS were retrospectively analyzed. Predictors of false-negative outcomes were identified by logistic regression analysis.
Results and conclusion. Three predictors for false-negative outcomes were identified: central location of the lung tumor (OR 3.7/4.5/3.6 for EBUS, EUS and EUS/EBUS respectively, $p < 0.05$), nodal enlargement on CT (OR 3.2/2.5/4.9 for EBUS, EUS and EUS/EBUS respectively, $p < 0.05$) and FDG-avidity of N2/N3 lymph node stations on PET (OR 4.2/4.0/7.5 for EBUS, EUS and EUS/EBUS respectively, $p < 0.05$). One subgroup (peripheral lung tumor, nodal enlargement on CT without FDG-avidity for N2/N3) had a low predicted probability (7.8%) for false-negative EUS. For combined EUS/EBUS, two subgroups were identified: peripheral located tumor with nodal enlargement on CT but without FDG-avidity for N2/N3 (predicted probability 4.7%) and centrally located tumor without affected lymph nodes on CT or PET (predicted probability 3.4%). In conclusion, for specific well-defined subsets of NSCLC patients the low predicted probability of metastasis after negative endosonography might justify omitting confirmatory surgical staging.

Rapid Diagnosis of Infection in the Critically Ill, a Multicenter Study of Molecular Detection in Bloodstream Infections, Pneumonia, and Sterile Site Infections

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Objective. Early identification of causative microorganism(s) in patients with severe infection is crucial to optimize antimicrobial use and patient survival. However, current culture-based pathogen identification is slow and unreliable such that broad-spectrum antibiotics are often used to insure coverage of all potential organisms, carrying risks of overtreatment, toxicity, and selection of multidrug-resistant bacteria. We compared the results obtained using a novel, culture-independent polymerase chain reaction/electrospray ionization-mass spectrometry technology with those obtained by standard microbiological testing and evaluated the potential clinical implications of this technique.
Design. Observational study.
Setting. Nine ICUs in six European countries.
Patients. Patients admitted between October 2013 and June 2014 with suspected or proven bloodstream infection, pneumonia, or sterile fluid and tissue infection were considered for inclusion.
Interventions. None.
Measurements and Main Results. We tested 616 bloodstream infection, 185 pneumonia, and 110 sterile fluid and tissue specimens from 529 patients. From the 616 bloodstream infection samples, polymerase chain reaction/electrospray ionization-mass spectrometry identified a pathogen in 228 cases (37%) and culture in just 68 (11%). Culture was positive and polymerase chain reaction/electrospray ionization-mass spectrometry negative in 13 cases, and both were negative in 384 cases, giving polymerase chain reaction/electrospray ionization-mass spectrometry a sensitivity of 81%, specificity of 69%, and negative predictive value of 97% at 6 hours from sample acquisition. The distribution of organisms was similar with both techniques. Similar observations were made for pneumonia and sterile fluid and tissue specimens. Independent clinical analysis of results suggested that polymerase chain reaction/electrospray ionization-mass spectrometry technology could potentially have resulted in altered treatment in up to 57% of patients.
Conclusions. Polymerase chain reaction/electrospray ionization-mass spectrometry provides rapid pathogen identification in critically ill patients. The ability to rule out infection within 6 hours has potential clinical and economic benefits.

The Association Between Heroin Inhalation and Early Onset Emphysema

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Background. Inhalation/smoking has become the most common method of recreational opiate consumption in the United Kingdom and other countries. Although some heroin smokers appear to develop COPD, little is known about the association.
Methods. We present data from a cohort of 73 heroin smokers with clinician-diagnosed and spirometrically confirmed COPD, seen within our clinical service, where symptoms developed before the age of 40 years.
Results. The whole group mean age at diagnosis was 41 years, subjects had smoked heroin for 14 years, and mean FEV1 was 1.08 L (31.5% predicted), with mean FEV1/FVC of 0.4. No subject was found to have severe α1-antitrypsin deficiency. Forty-four subjects had either a high-resolution CT (HRCT) scan (32) or measurement of lung diffusion (12). Overall HRCT scan emphysema score averaged across the upper, middle, and lower part of the lung was 2.3 (5%-25% emphysema), with 47% subjects having an upper lobe emphysema score $\geq$ 3 (25%-50% emphysema). Median diffusing capacity of the lung for carbon monoxide was 48% of predicted value.
Conclusions. Recreational smoking of heroin appears to lead to early onset COPD with a predominant emphysema phenotype. This message is important to both clinicians and the public, and targeted screening and education of this high-risk population may be justified.

Divergent Epidermal Growth Factor Receptor Mutation Patterns Between Smokers and Non-smokers with Lung Adenocarcinoma

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Introduction. Smoking status is an important determinant of the prevalence of epidermal growth factor receptor (EGFR) mutations in lung cancer patients. However, it is unclear whether smoking status could also influence the spectrum of EGFR mutations.
Methods. We enrolled patients with lung adenocarcinoma from three medical centers in Taiwan. EGFR mutations were assessed by Sanger direct sequencing. The objective of this study was to evaluate the influence of smoking status on both the frequency and patterns of EGFR mutations.
Results. From 2001 to 2013, a total of 1175 patients with lung adenocarcinoma were enrolled for EGFR mutation analysis. The overall EGFR mutation rate was 59.6%, which was significantly higher in females than males (69.1% vs. 49.8%) and in non-smokers than current/former smokers (73.8% vs. 29.8%) (both $P < 0.001$). Among patients harboring EGFR mutations, smokers expressed L858R mutation less frequently (35.2% vs. 50.2%, $P = 0.005$) and exon 19 deletions more frequently (52.8% vs. 38.8%, $P = 0.008$) than non-smokers. Smokers and non-smokers also had divergent exon 19 deletions subtypes (Del E746-A750 82.5% vs. 57.6%, respectively, $P < 0.001$). Among subgroup patients harboring the L858R mutation, smokers were associated with a higher rate of complex mutations than non-smokers (34.2% vs. 8.4%, $P < 0.001$).
Conclusions. Our results suggested that smoking status could influence not only the frequency but also the spectrum of EGFR mutations. These findings provide a clue for further investigation of EGFR mutagenesis.

Non-small Cell Lung Cancer Patients with Brain Metastases Treated with First-line Platinum-doublet Chemotherapy: Analysis from the European FRAME Study

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Objectives. We report on a post-hoc analysis of patients with brain metastases from a large prospective observational study of first-line treatment of non-small cell lung cancer (NSCLC). The aim was to describe baseline characteristics of NSCLC patients with brain metastases, understand their first-line treatment and report outcomes attained in real-world settings.
Materials and Methods. This post-hoc analysis included all patients in the European observational FRAME study who had brain metastases at initiation of first-line treatment. Descriptive statistics were used for continuous and categorical variables and survival outcomes were assessed using the Kaplan-Meier approach.
Results. Our data showed that 17% of patients (263/1564) had spread of the disease to the brain at initiation of first-line treatment. Patients with brain metastases were slightly younger, and more likely to have NSCLC of non-squamous histology than the overall study sample. 34% had received prior palliative radiotherapy to the brain. Our analysis showed a median overall survival (OS) of 7.2 months [95% confidence interval (CI) 6.1-8.2] for all patients with brain metastases treated with first-line platinum-based chemotherapy, ranging from 5.6 months for those treated with gemcitabine plus platinum up to 9.3 months for those treated with pemetrexed plus platinum. Further analysis showed that patients with brain metastases were more frequently treated with pemetrexed platinum-doublet therapy than with any other regimen.
Conclusions. Our analysis provides a unique set of real-world data which adds to current understanding about treatment decisions and outcomes for NSCLC patients with brain metastases for whom there is little clinical trial data available.

Cytotoxic and Pro-apoptotic Activities of Leaf Extract of *Croton Bonplandianus Baill.* Against Lung Cancer Cell Line A549

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The acetone extract (AcE) of the *Croton bonplandianus* Baill., an exotic weed of the Euphorbiaceae family, was studied for cytotoxicity, apoptosis, cell cycle arrest in A549 cell line and antioxidant capacities using MTT assay, acridine orange/ethidium bromide (AO/EB staining), cell cycle analysis and DPPH radical scavenging assay, respectively. Based on the cytotoxic activity, the extract was tested for the apoptotic effect using AO/EB and Hoechst 33258 staining. The apoptosis was characterized by chromatin condensation and DNA fragmentation. Further, to determine the stage of cell death, cell cycle analysis was performed by flow cytometry and AcE was found to arrest G2/M phase in a dose dependent manner. The number of cells in G2/M phase increases with concurrent accumulation of cells in sub G0/G1 phase indicates the induction of apoptosis at G2M phase. The free radical scavenging activity of the AcE against DPPH was considerably significant. The cytotoxic, apoptotic and antioxidant effect of the AcE could be well correlated with the presence of potent free radical scavenging secondary metabolites such as phenols (43±0.05 ìg/mL), flavonoids (3.5±0.07 µg/mL) and tannin (0.36±0.1 µg/mL). Our study has shown that A549 cells were more sensitive to AcE with an IC_{50} of 15.68±0.006 µg/mL compared to the standard drug 2.20±0.008 µg/mL (cisplatin). The results suggest that *Croton bonplandianus* could serve as a potential source of alternative therapeutic agent for treating cancer. Further research is required to isolate the active principle compound and determination of its anticancer property.