6553 POSTER

Role of intraoperative ultrasound for mediastinal staging in lung cancer surgery

N. Ilic[1], A. Petricevic[1], J. Juricic[1], J. Banovic[1], A. Tripkovic[1], N. Frelta Ilic[2], I. Tripkovic[3]. [1]*University Surgical Hospital, Thoracic Surgery Department, Split, Croatia;* [2]*Policlinic Cito, Oncology Department, Split, Croatia;* [3]*Public Health Organization, Epidemiology Department, Split, Croatia*

Objectives: The extend of lymph node involvement in patients with non-small cell lung cancer (NSCLC) is the most important prognostic factor and influences multimodality treatment. We studied safety, accuracy and characteristics of intraoperative ultrasound (US) guided systematic mediastinal nodal dissection in patients with resected NSCLC.
Methods: Intraoperative hand held ultrasound probe was used in systematic mediastinal nodal dissection in 54 patients after radical surgery for NSCLC. Mapping of the lymph nodes by their number and station followed by histopathologic evaluation was performed. Data were compared with 58 patients who underwent lung resections and systematic mediastinal nodal dissection for NSCLC within the same time period at our institution. Statistical analysis was carried out.
Results: The surgical procedure used depended on the extent of the disease, as well as the cardiopulmonary reserve of the patients and was comparable in both groups. Operating time was prolonged for 12 (6−20) minutes in patients with US guided mediastinal nodal dissection, but number and stations of evaluated lymph nodes was significantly higher ($p > 0.001$) at the same group of patients. Skip nodal metastases were found in 24% of patients without N1 nodal involvement. Standard staging system seemed to be improved in US guided mediastinal lymphadenectomy patients. Complications rate showed no difference between analyzed groups of patients.
Conclusion: Higher number and location of analyzed mediastinal nodal stations in patients with resected NSCLC using hand held ultrasound probe suggested to be of great oncology significance. Procedure showed improved safety and higher accuracy. Our results indicate that intraoperative US may have important staging implication.

6554 POSTER

Serum sialyl Lewisx and cytokeratin 19 fragment as a predictive factors for recurrence in patients with stage I non-small cell lung cancer

S. Mizuguchi[1], N. Nishiyama[2], T. Iwata[2], T. Nishida[2], N. Izumi[2], T. Tsukioka[2], K. Inoue[1], S. Suehiro[3]. [1]*Bell Land General Hospital, Thoracic Surgery, Osaka, Japan;* [2]*Osaka Cty University Hospital, Thoracic Surgery, Osaka, Japan;* [3]*Osaka City University Graduate School of medicine, Cardiovascular Surgery, Osaka, Japan*

Background: Surgical treatment is the most efficient therapy for early non-small lung cancer (NSCLC). However, even after radical surgery many patients relapse or progress to systemic disease. Recurrence was detected in approximately 40−50% of patients with NSCLC, even in stage I. If there were a reliable marker that could predict recurrence, these patients may receive aggressive therapy to improve their survival rate. This study aimed to establish the clinical significance of preoperative serum cytokeratin 19 fragment (CYFRA21−1) and Sialyl Lewisx (SLX) in patients with stage I non-small cell lung cancer.
Material and Method: The study involved 137 patients (87 male, 50 female; median age 69 years) with completely resected stage I NSCLC. SLX, carcinoembryonic antigen (CEA), squamous cell carcinoma antigen (SCC), and CYFRA21−1 were examined. Receiver operator characteristic (ROC) curves were constructed to determine prognostic cut-off values.
Results: Among 137 patients, we identified 30 patients with recurrence within 3 year or earlier. The 5-year survival rates in patients with and without recurrence were 14%, and 81%, respectively. The serum concentrations of SLX, CEA and CYFRA21−1 in the recurrence group were significantly higher than those in the non-recurrence group. The areas under the ROC curve (AUC) were 0.72, 0.65, 0.53, and 0.64 for SLX, CEA, SCC, and CYFRA21−1, respectively. The prognostic cut-off values, according to ROC curves, were 36 U/ml, 7.8 ng/ml, 1.5 ng/ml, and 3.2 ng/ml for SLX, CEA, SCC, and CYFRA21−1, respectively. A log-rank test revealed that age, performance status, T factor, SLX, CEA, SCC and CYFRA21−1 were associated with a significant survival rate. By multivariate analysis, age, performance status, SLX (risk ratio, 3.82) and CYFRA21−1 (risk ratio, 3.66) were independent prognostic factors. For patients positive for both CYFRA21−1 and SLX, the relative risk was 5.32 compared with patients who were negative for both markers. The 5-year survival rates were 80% in the group negative for both markers (n = 86); 52% in the group positive for one of the markers (n = 43); and 13% for the group positive for both markers (n = 8) ($p < 0.001$).
Conclusions: Serum SLX and CYFRA21−1 were prognostic markers for stage I NSCLC. Their combination should contribute to the classification of stage I NSCLC patients. We should consider adjuvant and neoadjuvant therapies to improve prognosis in patients positive for both tumor markers.

6555 POSTER

Treatment of thymomas and thymic carcinomas: a retrospective review of treatment outcomes at the Tom Baker Cancer Centre from 1982 to 2004

P. Wright[1], M. Eliasziw[2], G. Gelfand[3], S. Grondin[3], S. McFadden[3], D. Morris[4], A. Balogh[1]. [1]*Tom Baker Cancer Centre, Radiation Oncology, Calgary, Canada;* [2]*University of Calgary, Community Health Sciences, Calgary, Canada;* [3]*Foothills Medical Centre, Thoracic Surgery, Calgary, Canada;* [4]*Tom Baker Cancer Centre, Medical Oncology, Calgary, Canada*

Background: The purpose of this retrospective cohort study was to determine the treatment outcomes of patients with thymoma or thymic carcinoma at a single tertiary care referral centre.
Materials and Methods: Patients in Southern Alberta with a pathological diagnosis of thymoma or thymic carcinoma were identified using the Alberta Cancer Board cancer registry. The patients were separated into early (1982–1998) and late (1999–2004) cohorts. Retrospective data were collected to determine if changes in patient factors, treatment factors, and/or outcome had occurred over time. The impact of these factors on overall survival (OS), disease free survival (DFS), and cause specific survival (CSS) were analyzed using the Kaplan-Meier method and Cox Proportional Hazards regression. Analyses were restricted to patients with Masaoka stage II-IV.
Results: A total of 62 patients were analyzed (thymoma n = 57, thymic carcinoma n = 5). There were fewer patients in the early cohort (n = 23) compared to the late cohort (n = 39). There were 30 stage II, 11 stage III, 17 stage IVA, and 4 stage IVB patients. Surgical extent varied from complete resection in 58% (36) to partial resection or biopsy in 42% (26). Curative intent radiation therapy to the primary tumor was delivered to 74% (46) with doses from 28−60 Gy (median dose 50 Gy) in 14−33 fractions. Curative-intent chemotherapy was used in 29% (18) with most patients (11) receiving standard CAP chemotherapy over 1−5 cycles (median 4 cycles). Sequential chemotherapy and radiation therapy was used in 22% (14) of which 64% (9) were Stage IV. The 5-yr OS for all patients was 60% (95% CI: 45.2−72.5%). There was a significant ($p = 0.034$) difference in 5-yr OS between the early group 46.0% (95% CI: 24.9−64.8%) and the late group 70.1% (95% CI: 48.4−84.1%). This finding was supported by Cox regression (HR 0.35, 95% CI: 0.12−1.05, $p = 0.061$). Using Cox regression, patients with stage III and IV were 4.7 times more likely to die by 5-yrs than stage II patients (95% CI: 1.38−16.2, $p = 0.013$). Similar findings for CSS were observed.
Conclusion: A trend towards improved 5-yr overall survival in the late cohort was seen independent of stage. This may reflect the use of multi-modality approaches to the treatment of thymic neoplasms. Our study also confirms that the most significant predictor of mortality at 5 years was Masaoka stage greater than II.

6556 POSTER

Prognostic role of standard uptake value (SUV) on positron emission tomography with ^{18}F-fluorodeoxyglucose (FDG-PET) in malignant pleural mesothelioma (MPM)

G.L. Ceresoli[1], C. Pinto[2], G. Selvaggi[3], P.A. Zucali[1], V. Mutri[2], S. Salamina[1], S. Fanti[4], A. Martoni[2], G.V. Scagliotti[3], A. Santoro[1]. [1]*Istituto Clinico Humanitas, Oncology, Rozzano (Milan), Italy;* [2]*Policlinico S.Orsola-Malpighi, Oncology, Bologna, Italy;* [3]*San Luigi Hospital University, Clinical & Biological Sciences, Turin, Italy;* [4]*Policlinico S.Orsola-Malpighi, Nuclear Medicine, Bologna, Italy*

Background: Previous studies have suggested that baseline maximal SUV independently predicts survival in MPM. Aim of this study was to confirm these results in a series of MPM patients (pts) treated with chemotherapy.
Materials and Methods: From July 2002 to October 2006, 63 pts underwent pre-treatment FDG-PET at three different Institutions. All pts were treated with chemotherapy, mainly pemetrexed-based, and were considered for extrapleural pneumonectomy (EPP) if they had resectable disease. Quartile and median values, as well the previously reported cut-off of 10, were considered to classify pts as low vs high SUV. SUV values were analyzed according to age, gender, histology (epithelial vs. non-epithelial), IMIG stage (I-II vs. III-IV), and EORTC prognostic model (good vs. poor score). The impact of these variables on overall survival (Sv) was evaluated by univariate and multivariate analysis.
Results: Median SUV for all pts was 6.3 (with quartiles values of 4.5 and 9). No other variable was significantly related to SUV in univariate analysis. A significantly longer survival was observed in pts with epithelial histology

(22.3 vs 7.9 months, p=.002), with SUV < 4.5 (30.5 vs 14.3 months, p=.042) and SUV < 10 (20.2 vs 10.6 months, p=.043). In a multivariate analysis, SUV > 4.5 and non-epithelial histology were associated to poor prognosis, with an hazard ratio (HR) of death of 2.48 (95% CI 1.03−5.94) and 3.72 (95% CI 1.54−9.01), respectively. SUV > 10 had borderline significance (HR 1.97, 95% CI 0.99−3.91).
Conclusions: SUV greater than 4.5 and non-epithelial histology were poor risk factors in our series of MPM patients. SUV > 10 had borderline significance. Baseline FDG-PET should be considered to stratify pts in clinical trials.

6557 POSTER

Second-line chemotherapy with gemcitabine and uracil/tegafur for relapsed or refractory non-small cell lung cancer: a phase II study

H. Tanaka[1], J. Tanaka[1], R. Itoh[1], H. Kuriyama[1], H. Kagamu[2], K. Itoh[3], K. Sato[4], K. Nakata[2], F. Gejyo[1], H. Yoshizawa[2]. *[1]Niigata University Medical and Dental Hospital, Division of Respiratory Medicine, Niigata, Japan; [2]Niigata University Medical and Dental Hospital, Bioscience Medical Research Center, Niigata, Japan; [3]Niigata Saiseikai Second Hospital, Niigata Lung Cancer Treatment Group, Niigata, Japan; [4]Nagaoka Red Cross Hospital, Niigata Lung Cancer Treatment Group, Nagaoka, Japan*

Background: Second-line chemotherapy with docetaxel has been shown to improve survival and quality of life (QoL) in patients with advanced non-small cell lung cancer (NSCLC). Gemcitabine (GEM) and uracil / tegafur (UFT) are both effective agents for NSCLC. The objectives of this study were to evaluate the efficacy, toxicity, and QoL status in NSCLC patients treated with GEM and UFT as second-line chemotherapy.
Methods: Patients with relapsed or refractory NSCLC, aged <80, with good performance status (PS) were eligible after giving informed consent. The treatment consisted of UFT (400 mg-2) on day 1 through 14 with intravenous infusions of GEM (900 mg-2) on day 8 and 15 of each 21-day cycle for up to 6 cycles of treatment. Common Terminology Criteria for Adverse Events v3.0 was used for toxicity assessment, and EORTC QLQ-C30/LC13 for QoL monitoring.
Results: Thirty-five patients with mean age of 61.7 years were enrolled. Twenty-five were male, and 10 were female. Twenty-two/11/1/1 patients had adenocarcinoma/squamous cell carcinoma/large cell carcinoma/ unclassified carcinoma, respectively. Total number of delivered courses was 97, with an average of 2.8 courses per patient. Overall response rate was 20% with 7 partial-response and 14 stable-disease. Median survival time was not yet reached with median follow-up period of 10.5 months. Median duration of response was 6.6 months. Grade 3 or 4 hematological toxicities included leukopenia in 10 patients, neutropenia in 14 patients, anemia in 5 patients, and thrombocytopenia in 3 patients. Three grade 3 diarrhea and 2 grade 3 febrile neutropenia were also reported. QLQ-C30 results showed that the patients maintained the baseline in global health status / QoL and functional scales with significant reduction of pain, insomnia, and financial difficulties in symptom scales / items after treatment. QLQ-LC13 also showed significant improvement of pain in other parts and worsening of peripheral neuropathy.
Conclusions: The GEM and UFT combination is well tolerated with comparable activity as second-line chemotherapy in relapsed or refractory NSCLC patients, and QoL assessment revealed symptomatic efficacy of this treatment.

6558 POSTER

Pharmacoeconomic analysis of erlotinib as second-line treatment of advanced non-small cell lung cancer in Taiwan

T. Hsia[1], G. Chang[2], Y. Chen[3], M. Lin[4], W. Su[5], C. Tsai[3], C. Tsai[6], L. Yang[6]. *[1]China Medical University Hospital, Department of Pulmonary Medicine, Taichung, Taiwan; [2]Taichung Veterans General Hospital, Department of Pulmonary Medicine, Taichung, Taiwan; [3]Taipei Veterans General Hospital, Chest Department, Taipei, Taiwan; [4]Chang Guang Memorial Hospital Kaohsiung Branch, Department of Pulmonary and Critical Care Medicine, Kaohsiung, Taiwan; [5]National Cheng Kung University Hospital, Tainan, Taiwan; [6]Roche Products Ltd., Pharma Department, Taipei, Taiwan*

Background: Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer-related mortality in Taiwan. Oral erlotinib offers proven efficacy by prolonging survival, delaying disease progression, and improving tumor-related symptoms as well as quality of life in previously treated patients with NSCLC. The objective of this pharmacoeconomic analysis is to access the cost-effectiveness of erlotinib compared to docetaxel and pemetrexed as second-line treatment of advanced NSCLC in Taiwan from payer's [Bureau of National Health Insurance (BNHI)] perspective.
Methods: A health state-transition economic model was developed to estimate incremental cost impact and the effectiveness in terms of quality-adjusted life years (QALYs). Clinical outcomes were derived from the pivotal trial of erlotinib vs. best supportive care (BR.21). Progression-free survival and post-progression were modeled by applying the actuarial method of Kaplan-Meier analysis with a monthly time scale of 24 months. Direct medical costs associated with drugs and drug administrations were calculated from the 2006 BNHI Fee Schedule. Resource utilizations and adverse events management were based on an expert panel survey conducted among 6 expert oncologists in Taiwan. Health-related utility scores were obtained from a utility study conducted among 154 people in the UK by applying the EQ-5D York tariff and the EQ-5D visual analogue scales. Incremental cost-effectiveness ratios (ICER) were calculated by applying a 5% discount rate. One-way sensitivity analyses were performed on key model parameters.
Results: Compared to docetaxel vs. pemetrexed, erlotinib demonstrates significant overall cost savings of NTD$8,446 vs. NTD$118,932 with survival benefits of 0.046 vs. 0.036 QALYs respectively. The ICER of erlotinib vs. docetaxel ranges from dominant (lower cost, better survival) to NTD$24,838/QALY for extended treatment duration. Erlotinib remains dominant compared to pemetrexed throughout sensitivity analysis.
Conclusions: From a Taiwan BNHI perspective, this pharmacoeconomic analysis shows that the use of erlotinib as second-line treatment of advanced NSCLC would not only save direct medical costs but also improve health outcomes compared to docetaxel and pemetrexed.

6559 POSTER

A prognostic index (PI) for predicting lung cancer patients with multiple brain metastases who may not benefit from whole brain radiotherapy (WBRT) due to early death

P. Sundaresan[1], R. Yeghiaian-Alvandi[1], V. Gebski[2]. *[1]Westmead Hospital, Radiation oncology, Sydney, Australia; [2]NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia*

Background: Palliative WBRT is often recommended in the management of multiple brain metastases. Time from initial assessment to benefit from WBRT may be as much as 6 weeks. Patients with a shorter survival may not benefit from WBRT. Identifying this group of patients at the time of assessment is difficult. The purpose of this study was to develop a PI that identifies those lung cancer patients with brain metastases who will not benefit from WBRT due to early death (death within 6 weeks).
Materials and Methods: The medical records of lung cancer patients who were to receive WBRT for multiple brain metastases over a 10-year period were reviewed and patients were classified as either having died within 6 weeks or having lived beyond 6 weeks. Potential prognostic indicators (age, ECOG performance status, weight loss >10%, histology, primary disease control and systemic disease status) were evaluated for correlation with death within 6 weeks of assessment. A PI was constructed by modelling the survival classification to determine the contribution of these factors towards a shortened survival.
Results: Of the 275 patients recommended to have WBRT for the management of multiple brain metastases from lung cancer, 64 (23.22%) died within 6 weeks. Prognostic factors predicting early death were performance status (ECOG > 2) and systemic disease status. Patients with a high PI score (>13) were at higher risk of death within 6 weeks.
Conclusion: 23% of patients died prior to benefit from WBRT. ECOG performance status and systemic disease status were the most predictive for early death. The PI may ultimately be a valuable decision tool for recommending WBRT for individual lung cancer patients with multiple brain metastases. Further validation is required to ensure the accuracy of this PI.