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Background: Malignant pleural mesotheliomas (MPMs) is a fatal disease mainly caused by past exposure to asbestos. MPMs are classified into three main histological subtypes: epithelioid, sarcomatoid, and biphasic type. There have been known several immunopathological markers for diagnosing MPMs, but there are not enough reliable markers, which often makes it difficult to diagnose MPMs correctly. In the present study, we investigated whether Claudin15 serves as a diagnostic and therapeutic target for MPMs. Claudins are four-transmembrane proteins and form a protein family consisting 27 members in humans. Specific combination of claudins are differentially expressed in different organs and form tight junctions with different permeability. Expression of Claudin15 has been known to be increased at mRNA level in MPMs. **Method:** Since 2003 to 2018, 34 patients were diagnosed with MPMs in our hospital. We made a new anti-Claudin15 rat monoclonal antibody, and established a hybridoma clone suitable for IHC. We immunostained 34 tissues with newly established anti-Claudin15 antibody, and compared the staining intensity and occupation with those of Calretinin, a known marker for MPMs. We also immunostained poorly differentiated lung adenocarcinomas, which are sometimes hardly distinguishable with MPMs, with anti-Claudin15 antibody to examine whether Claudin15 staining can distinguish MPMs from adenocarcinomas. **Result:** Of the 34 cases, the epithelial type was 27 cases, the sarcomatoid type was 1 case, and the biphasic type was 6 cases. The overall expression rate was 53% for Claudin15 and 59% for Calretinin. In terms of histology type, Claudin15 was 50% and Calretinin was 65% in the epithelial type, while Claudin15 was 80% and Calretinin was 40% in the biphasic type. There was only one sarcomatoid type, neither was expressed. Poorly differentiated adenocarcinomas showed no or very low-level expression of Claudin15. **Conclusion:** Our results suggest that Claudin15 could be a novel diagnostic marker for MPMs, especially for biphasic type. Greater number of cases and further analyses would be required to establish Claudin15 as a diagnostic impact for MPMs in clinical use. **Keywords:** malignant pleural mesothelioma, Claudin, tight junctions

P2.06-21

Efficacy and Safety of Tumor Treating Fields Delivery to the Thorax by Computational Simulations



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Background: Tumor Treating Fields (TTFields), an anti-mitotic therapy low intensity, intermediate frequency, alternating electric fields, are approved for glioblastoma. The STELLAR phase 2 registration trial recently demonstrated a significant extension in overall survival in mesothelioma patients treated with TTFields and standard of care chemotherapy vs historical control data on chemotherapy alone. The results highlight the potential benefit of TTFields to treat cancer located in the thorax. Preclinical studies show that efficacy increases with the intensity of the electric field. Optimizing treatment requires a thorough understanding of how TTFields distribute within the body. Simulations can be used to evaluate the treatment safety by assessing tissue heating associated with absorption of the electric field. We present a simulation based study on field distribution and associated heating when delivering TTFields to the thorax. **Method:** We delivered TTFields to the thorax of realistic computational phantoms of a male, female, and obese male (ZMT, Zurich, Switzerland). The field was delivered to the computational phantoms using transducer arrays similar to those used to deliver TTFields to the thorax with the NovoTTF-100L. The field intensities within the lungs of the models were evaluated. Specific Absorption Rate (SAR), a metric for assessing heating due to electromagnetic absorption, was calculated. **Result:** The highest field intensities within the lungs were obtained when the arrays were axially-

aligned with the parenchyma as anatomically possible. Field intensities throughout the lungs exceeded the therapeutic threshold of 1 V/cm in all models. Within the internal organs, SAR values were below the allowed level of 10 W/kg set out in the ICNIRP guidelines for occupational exposure. Maximum SAR levels did not exceed 20 W/kg. Occupational exposure standards typically incorporate a safety factor of around 10 when setting basic restrictions, therefore this level of SAR is considered safe and unlikely to lead to heat-related tissue damage. **Conclusion:** TTFields can be delivered to the lungs at therapeutic levels that do not cause damage through tissue heating. **Keywords:** Tumor Treating Fields, Efficacy, Safety

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Is Laboratory Prognostic Index a Valuable Prognostic Index for Malignant Pleural Mesothelioma?



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Background: Prognostic significance of Laboratory Prognostic Index (LPI) was demonstrated in non-small cell lung cancer before. We aimed to assess the prognostic value of LPI in patients with malignant pleural mesothelioma (MPM). **Method:** Records of MPM patients were examined retrospectively for serum laboratory results at diagnosis along with demographical and clinicopathological features. LPI is consisted of white blood cell count ($>10000/\text{mm}^3$), albumin ($<3.5 \text{ g/dL}$), lactate dehydrogenase ($>248 \text{ U/L}$), alkaline phosphatase ($>120 \text{ U/L}$) and calcium ($>10.5 \text{ mg/dL}$) levels; and it is graded according to the number of abnormal parameters: 0 (none), 1 (one) and 2 (two or more). Kaplan-Meier method and stratified log-rank test were used in univariate analysis and a Cox regression model was conducted to determine independent predictors of overall survival (OS). **Result:** Sixty-one patients were included in the study. Median age at diagnosis was 59 (51-66) years. 45 deaths (73.8%) have occurred at the time of final analysis and median OS was 19.5 months. One-year survival rates for patients with LPI 0, 1 and 2, were 82%, 61% and 59%; 2-year survival rates were 75%, 47% and 24%, respectively. Median OS of patients with LPI 0, 1 and 2 were 36.5, 21.7 and 15.6 months, respectively ($p=0.007$). Age, ECOG performance status, histology, hemoglobin level and LPI were found to effect OS significantly or to have a trend ($p<0.1$). In multivariate analysis, LPI ($p=0.033$) and ECOG performance status ($p<0.001$) were the independent prognostic factors. **Conclusion:** The LPI may be a valuable prognostic factor in mesothelioma as well. Larger studies are needed to confirm this result.

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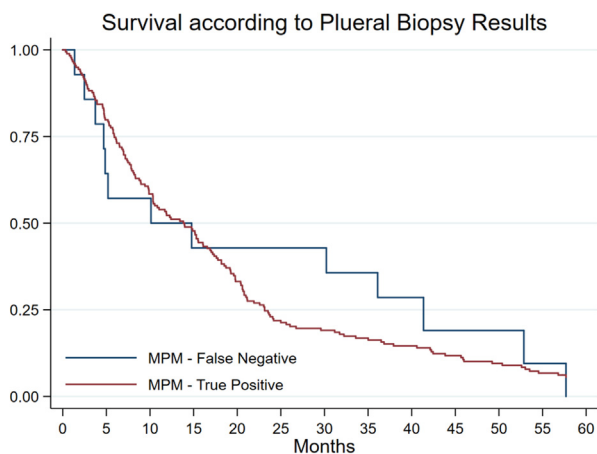
The Accuracy of Video-Assisted Thoracic Surgery Pleural Biopsy in Patients with Suspected Malignant Pleural Mesothelioma: A Real-Life Study



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Background: The heritage of occupational and environmental asbestos exposure in Piedmont, Italy, is an enduring epidemic of malignant pleural mesothelioma (MPM). Pleural biopsy (PB) performed *via* thoracoscopy (or video-assisted thoracic surgery (VATS)) remains the diagnostic gold standard for patients with suspected mesothelioma. The aim of our study was to investigate the accuracy of PB *via* VATS and to analyze the diagnostic path of the patients who experienced an initial MPM misdiagnosis. **Method:** Patients who underwent PB by VATS for suspected MPM from 2004 to 2013 were analyzed. The Registry of Malignant Mesothelioma (RMM) records were examined to crosscheck incident cases and to recognize misdiagnosed MPM. Sensitivity and specificity of the initial PB assessment versus the final classification of cases by RMM were evaluated. Overall survival (OS) was estimated using the Kaplan-Meier method and compared using log-rank test.



Result: Data of 552 patients were analyzed. Of those, MPM was diagnosed in 178 cases (32%) and no false-positive PBs were observed. Sensitivity and specificity were 93% and 100%, respectively. The number of false-negative PBs was 14 (2%). Of those, 10 (71%) had an initial diagnosis of chronic pleuritis, 3 (28.5%) of atypical mesothelial proliferation and 1 had reactive mesothelial proliferation. All of them reported a history of asbestos exposure and the correct diagnosis was reached after a median of 160 days (interquartile range 86-243) as follow: 9 (64%) after a further PB by VATS, 3 (22%) by cytology examination of a pleural effusion, 1 (7%) by fine-needle biopsy and 1 (7%) by open surgery. The median survival time of the patients with eventual MPM diagnosis was 13.8 months (CI 95%: 10.3-16.6). One- and 4-year survival were 52% and 10% in MPM PB positive cases and 50% and 19% in false-negative cases ($P=0.66$) (Figure 1). **Conclusion:** When a history of asbestos exposure is reported and a strong clinical suspicion persists after a negative PB, iterative biopsy attempts should be considered. In high-volume centers, MPM misdiagnosis rate remains small and future advancement in diagnostic technologies could further increase the accuracy of diagnosis. **Keywords:** Mesothelioma, Pleural biopsy, False negative

Background: Malignant pleural mesothelioma (MPM) is a rare but lethal tumour arising in the 5th – 7th decade of life of predominantly male industrial workers of developed countries. The prognosis is dismal because of early spreading and scarcity of therapies. Surgery (extrapleural pneumonectomy or pleurectomy/decortication) has shown some improvement in patient survival, even more important with the addition of radio or chemotherapy. Patients unfit or with advanced disease are treated with palliative chemotherapy or palliative care alone. Some centres (or countries) don't have the resources to embark in such aggressive and expensive managements, pondering the idea that in mesothelioma patients, complex therapies are only a futility exercise not worth the investment in herculean surgery or costly and patient-consuming radio or chemotherapy. The question if aggressive therapy is superior to nihilist approaches in terms of survival (SV) is difficult to answer but of critical importance in developing countries. **Method:** Consecutive patients pathologically diagnosed with MPM of 2 health centres in the same city and time frame were assessed. Centre A is a public Hospital with an assigned population of 1 million, without thoracic surgeon and oncologic committee, and patients were seldom referred to palliative chemotherapy. Centre B is a tertiary, referral academic university Hospital with Thoracic surgeons and oncologic committee. Centre A had 10 patients reviewed and centre B 20. Both cohorts were examined in terms of treatment and SV. **Result:** The 2 series were comparable in terms of age (median=61,5) and sex (masculine: 70% for Centre A, 80% for Centre B). Centre A had 30% of patients with presence of metastasis at the time of diagnosis, while centre B had 10%. In centre A 2 of 10 patients received chemotherapy. In centre B: 9 patients had aggressive surgery, 7 patients received chemotherapy and 2 patients received radiotherapy. Kaplan Meier estimate showed 12-month SV of 51% (CI95% 16-79) in centre A and 59% (CI95% 35-77) in centre B, but there were no statistical differences between both groups. **Conclusion:** Few patients were diagnosed (30 overall) in line with Chilean epidemiology. The 2 centres had radically different resources and approaches to treat this illness, however, even though there is a tendency towards better survival in Centre B, there were no statistically differences between both groups. Differences could appear increasing the follow-up time or including more centres, alternatively, the rarity of this disease could produce oncologic teams with not enough experience dealing with it affecting survival outcomes. **Keywords:** Mesothelioma, Survival, treatment

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Mesothelioma Survival in 2 Health Centres in Santiago de Chile



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Mesothelioma UK Armed Forces Project: Establishing a National Support Service for Veterans / Armed Forces Personnel with Mesothelioma



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Background: In 2012 the UK Government announced that fines levied against banks for manipulating the London Inter-Bank Offered rate (LIBOR) rates would be used to support Armed Forces and emergency charities. In 2016 Mesothelioma UK (MUK) applied for a grant from this scheme to support a three year project to develop a specialist service for Armed Forces personnel and veterans affected by mesothelioma – the asbestos related cancer. **Method:** The aim of the project is to increase awareness and support for both serving and ex-military personnel who may have been exposed to asbestos. A work group which included representatives from MUK, patients/carers, advocacy groups and