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Title: Significance of age, tumor location and histological subtype in lung cancer with brain metastasis

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Body: Development of brain metastasis is common in lung cancer and influences both the quality of life and the overall survival of the patients. We studied the clinico-pathological data of 1025 patients, who had cytologically or histologically confirmed lung cancer. Of them 575 patients had brain metastasis that was diagnosed by CT scan or MRI. 450 patients, who did not develop cerebral metastasis during long-term follow up served as a control. Brain metastasis was found to develop more frequently in younger patients (59.5 years versus 62.2 years, $p<0.001$) and in females versus in males ($p<0.001$). In the metastatic group the most frequent histological subtype of lung cancer was adenocarcinoma (ADC) (47.3%) and small cell lung cancer (SCLC) (20.5%). On the contrary, in the control group the squamous cell carcinoma (SCC) (37.8%) was the most common type. Patients with ADC was younger when brain metastasis was present, than in the control group (58.9 years, versus 62.0 years, $p<0.001$). Development of brain metastasis was significantly more frequent in tumors of the central airways ($p<0.001$). In case of brain metastatic ADCs and SCCs the location of the primary tumor was more frequently in the central airways than in ADCs and SCCs without cerebral metastasis ($p<0.001$, $p=0.024$, respectively). Such a tendency was not observed in SCLC cases. More than half of the patients had multiple brain metastases (51.5%) that were found mainly in SCLC cases ($p=0.024$). Our results suggest that brain metastasis is more common in lung ADC and SCLC. Furthermore, patients with younger age, female gender and tumors in the central airways have a higher risk to develop brain metastasis.