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Surgical Outcome in Early Stage Small Cell Lung Cancer



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Background: Chemo-radiation is considered to be the standard treatment for the management of limited disease of small cell lung cancer (SCLC). Even in this early stage, the role of surgery in SCLC is still controversial. We sought to examine the role of surgery; complete resection in terms of survival in SCLC. **Method:** A retrospective review was undertaken of patients who underwent surgery for SCLC between 2001 and 2015. Patients were staged according to the 7th edition of the Tumor, Node, Metastasis classification of lung cancer. Actuarial survival estimated with Kaplan Meier method and comparisons were undertaken using Cox regression hazard model. Clinicopathological factors and predictors of survival were analyzed. **Result:** We identified 49 patients who underwent complete resection. The mean follow up period was 1343 days. The mean age was 70.7 years. 40 patients were men and 9 were women. The number of patients of clinical stage was stage IA :21, IB: 15, IIA: 4, IIB: 6, IIIA:3. Operative procedure was lobectomy in 43, segmentectomy in 1, wedge resection in 5. The number of patients of pathological stage was stage IA :15, IB: 11, IIA: 14, IIB: 7, IIIA:2. Adjuvant chemotherapy was performed in 26 patients (53.1%). The 5-year overall survival (OS) rate in all patients was 58.8%. The 5-year OS was 61.3% in c-stage I, 54.5% in c-stage II, and 50% in c-stage III. The 5-year OS were 66.2% in p-stage I, 55.4% in p-stage II, and 50% in p-stage III. The 5-year OS of patients with adjuvant chemotherapy was significantly better than that of patients without adjuvant chemotherapy (77.8% vs. 39.8%, $p=0.005$). Multivariable Cox regression hazard model demonstrated that adjuvant chemotherapy was prognostic factor of overall survival (OS) (hazard ratio 0.255 (.095-.688), $p=0.007$) **Conclusion:** Surgical outcome for early stage SCLC was satisfied one. The role of surgery for this group seemed to be important. Adjuvant chemotherapy may improve prognosis and long-term survival will be expected. **Keywords:** chemotherapy, small cell lung cancer, Surgery

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The Addition of Antiangiogenic Agents to Chemotherapy for Patients with Extensive-Stage Small Cell Lung Cancer: A Meta-Analysis



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Background: The combination chemotherapy of etoposide and a platinum salt represents the standard therapy for almost 30 years in patients with ED-SCLC (extensive-disease small-cell lung cancer). While, the survival benefit of chemotherapy is not obvious. Antiangiogenic agents have been confirmed to have survival benefits for patients with NSCLC (non-small cell lung cancer). However, there is no established role for antiangiogenic therapy in SCLC. **Method:** we conducted this meta-analysis to evaluate antiangiogenic agents plus chemotherapy in patients with ED-SCLC. Pub-med, EMBASE, Cochrane Library and ClinicalTrials.gov website were systematically searched for RCTs (randomized controlled trials) that compared antiangiogenic agents plus chemotherapy with chemotherapy alone in ED-SCLC. **Result:** We firstly found that antiangiogenic agents plus chemotherapy was well tolerated and could provide a statistically significant improvement in PFS (progression-free survival) for patients with

ED-SCLC (HR = 0.76 [95% CI 0.65, 0.88], $P = 0.0003$). The results of ORR (objective response rate) (RR = 1.06 [95% CI 0.96, 1.18], $P = 0.23$) and OS (overall survival) (HR = 0.98 [95% CI 0.80, 1.21], $P = 0.85$) showed no benefit for antiangiogenic agents plus chemotherapy.

Conclusion: Our study firstly shows that the addition of antiangiogenic agents to standard chemotherapy is well tolerated and can provide a statistically significant improvement in PFS for patients with ED-SCLC. Further, maintenance therapy with antiangiogenic agents is an effective treatment option for ED-SCLC patients who received four to six cycle of chemotherapy. Additionally, four-drug chemotherapy plus antiangiogenic agents may be better for ED-SCLC patients with PS of 1 to 2. However, whether antiangiogenic agents plus chemotherapy can influence OS for ED-SCLC needs further validation. **Keywords:** small cell lung cancer, chemotherapy, antiangiogenic agents

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Case Series of Small Cell Lung Cancer Transformation as Resistance Mechanism to Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitor



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Background: Patients with epidermal growth factor receptor (EGFR) mutant advanced non-small cell lung cancer (NSCLC) developed resistance to first- or second-generation EGFR-tyrosine kinase inhibitor (TKI) after 9-13 months and third-generation EGFR-TKI after 10 months, respectively. Small cell lung cancer (SCLC) transformation is a rare resistance mechanism in these patients. **Method:** Tissue re-biopsy was performed in 35 patients with EGFR mutant advanced NSCLC who failed first-line EGFR-TKI; and 4 patients with acquired T790M mutant advanced NSCLC who failed third-generation EGFR-TKI, to look for SCLC transformation. **Result:** SCLC transformation was identified in 2 out of 35 (5.7%) patients who failed first-line EGFR-TKI and 1 out of 4 (25.0%) patients who failed third-generation EGFR-TKI. The first patient was a 70-year-old never-smoker male who was diagnosed with stage IV lung adenocarcinoma harboring exon 19 deletion mutation in April 2014. He had partial response (PR) to gefitinib 250 mg daily but developed symptomatic progressive disease (PD) after 26 months. Re-biopsy of his enlarging primary lung lesion showed SCLC transformation. The second patient was a 43-year-old never-smoker male who was diagnosed with stage IV lung adenocarcinoma harboring exon 19 deletion mutation in November 2015. He had PR to gefitinib 250 mg daily but developed symptomatic PD after 15 months. Re-biopsy of his rapidly enlarging primary lung lesion showed SCLC transformation. His plasma cell-free tumor DNA (ctfDNA) was positive for T790M mutation. The third patient was a 62-year-old never-smoker female who was diagnosed with stage IV lung adenocarcinoma harboring exon 21 L858R mutation in November 2015. She had PR to gefitinib 250 mg daily but experienced symptomatic PD after 8 months' of gefitinib therapy. Re-biopsy of her primary lung tumor revealed the presence of T790M mutation and her treatment was switched to osimertinib 80 mg daily. After an initial PR, she developed PR in the 12th month of osimertinib treatment. Biopsy from a metastatic inguinal lymph node showed SCLC. The first and second patients were given standard SCLC chemotherapy with carboplatin and etoposide but did not respond. The third patient sought treatment in another hospital. **Conclusion:** Re-biopsy is recommended in all patients with symptomatic PD while on EGFR-TKI treatment. SCLC transformation under the pressure of first, second and third-generation EGFR-TKI is an emerging challenge to the management of advanced NSCLC. Other than conventional carboplatin and etoposide chemotherapy, new treatment strategies should be explored to improve the outcome of patients who develop SCLC transformation. **Keywords:** Epidermal growth factor receptor, resistance mechanism, small cell lung cancer