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Review article

Treatment of Non-small Cell Lung Carcinoma in Early Stages[☆]

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Treatment of lung carcinoma is multidisciplinary. There are different therapeutic strategies available, although surgery shows the best results in those patients with lung carcinoma in early stages. Other options such as stereotactic radiation therapy are relegated to patients with small tumours and poor cardiopulmonary reserve or to those who reject surgery. Adjuvant chemotherapy is not justified in patients with stage I of the disease and so double adjuvant chemotherapy should be considered. This adjuvant chemotherapy should be based on cisplatin after surgery in those patients with stages II and IIIA.

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Tratamiento del carcinoma broncogénico de célula no pequeña en estadios precoces

R E S U M E N

El tratamiento del carcinoma broncogénico es multidisciplinar. Se dispone de diferentes estrategias terapéuticas, siendo la cirugía la que presenta mejores resultados en aquellos pacientes con carcinoma broncogénico en estadios precoces. Otras opciones como la radioterapia estereotáctica quedan relegadas a pacientes con pequeños tumores y mala reserva cardiopulmonar, o a aquellos que rechacen la cirugía. La quimioterapia adyuvante no está justificada en pacientes con enfermedad en estadio I, planteándose doble quimioterapia adyuvante basada en cisplatino tras la cirugía en aquellos con estadios II y IIIA.

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Table 1 – Prognosis According to Lung Cancer Stage.

Stage	GS 5y %	Local recurrence/distance %
IA	67	10/15
IB	57	10/30
IIA	55	12/40
IIB	39	
IIIA (T3N1M0)	25	15/60

Non-small cell lung cancer (NSCLC) accounts for 85% of lung carcinomas. The therapeutic goals depend on the disease stage at the time of diagnosis. For patients in stages I, II, and III, the goal is cure. For patients in stage IV, the goal is to alleviate symptoms and prolong survival.

Bronchogenic carcinomas are considered to be in the initial stages when the tumour is localised within the lung, with or without affecting the hilar lymph nodes (stages I and II and some cases of IIIA). The 5-year survival rate of patients with pathological stage IA is 67%; stage IB, 57%; and stage IIIA, 25%¹ (Table 1).

The therapeutic options for NSCLC in stages I and II are mainly local (surgery, conventional radiotherapy [RT], stereotactic body radiotherapy [SBRT], radiofrequency ablation [RFA], cryosurgery, and brachytherapy). Few cases are treated with adjuvant chemotherapy.

Surgical Treatment

It is estimated that approximately 20% of bronchogenic carcinoma patients are diagnosed at an early stage. The therapeutic objective in these patients is to cure the disease, which is achieved in 60%–80% of patients in stage I and in 40%–50% of patients in stage II.

Lobectomy

The most important curative therapy for these cases is surgery, which can encompass lobectomy or tumorectomy, depending on the T and N extension grades of the tumour.

Since 1995, it has been assumed that sub-lobular resections have worse results in terms of local recurrence (three-fold) and 5-year survival rate (30% less) compared with lobectomies. These data were obtained from a randomised clinical study conducted by Ginsberg in 247 patients with stage IA NSCLC who randomly underwent either a lobectomy or a sub-lobular resection (segmentectomy or wedge resection).² A 4–5-year follow-up was conducted. However, there was no further discussion on which patients underwent segmentectomy and which patients underwent wedge resection (with worse results). Progression control was conducted using chest Rx, which did not diagnose early recurrence in the lobectomy cases. The statistical analysis has also been criticised. After a statistical revision in 2003 by Patel, no significant differences were found in the 5-year survival rates.³

In 1995, Martini published the results from 598 stage I NSCLC patients who underwent surgery at Memorial Sloan Kettering Hospital over a 15-year period. Of these patients, 4% underwent pneumonectomy, 85% underwent lobectomy, and

11% underwent sub-lobular resection. Only patients who could not tolerate a more extensive surgery underwent sub-lobular resections, which had a 50% recurrence index. However, in the cases where appropriate staging was conducted via lymphadenectomy, the recurrence rate was found to be only 5%. Furthermore, tumour size was also identified as a risk factor for recurrence. The 5-year survival rate for sub-lobular resections was 59%, whereas the rate for lobectomies/pneumonectomies reached 77%.⁴

Similar results were published in a study conducted at the Mayo Clinic in 2002. This study compared results from 100 patients with stage I NSCLC and $T \leq 1$ cm who underwent either a lobectomy, bi-lobectomy, segmentectomy, or wedge resection. The 5-year survival rate was 92% for lobectomies and 47% for sub-lobular resections. Interestingly, when the sub-lobular resections were examined, the anatomical segmentectomies had a 75% survival rate compared with only 42% for wedge resections. In fact, no significant differences were found between anatomical segmentectomies and lobectomies.⁵

More recently, in December of 2011, Whitson et al. at the University of Minnesota conducted a retrospective study assessing 6810 bronchoalveolar adenocarcinoma patients who had undergone lung resection (anatomical segmentectomy, wedge resection, or lobectomy). The authors concluded that lobectomies had the best outcomes in all cases. After the data were adjusted for confounding factors and tumour characteristics for each patient, it was found that both anatomical segmentectomy and lobectomy had similar results. This was not the case for wedge resections. The results were also independent of age, gender, tumour size, and degree of differentiation.⁶

Sub-lobular Resections

Due to an improvement in diagnostic techniques, small and peripheral lesions are more frequently diagnosed than more advanced tumours. These lesions are easier to excise by segmentectomy. For this reason, other analyses have been conducted to compare these therapeutic options.

In 1995, Landrenau published an interesting multicentre analysis using a non-random and prospective comparison of stage I NSCLC cases treated with lobectomies with cases that underwent open wedge resection or videothoracoscopy. Of the 219 patients studied, 117 underwent lobectomies, and 102 underwent wedge resection. The local recurrence rate was 19% for sub-lobular resections and 9% for lobectomies. However, no statistically significant differences were found in terms of 5-year survival rates.

Moreover, when cancer-specific survival was taken into account, segmental resections were favoured, given the decrease in perioperative morbidity and mortality, especially in patients with insufficient cardio-respiratory reserve. Finally, the possibility of intraoperative RT for sub-lobular resection cases was discussed and could achieve better resection margins and decrease local recurrence.⁷

El-Sherif published a retrospective analysis in 2006 comparing 784 stage IA NSCLC patients who underwent lobectomies or segmentectomies and did not find any significant differences between the two treatments. Other retrospective

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