



Surgical treatment of stage IIIa non-small cell lung cancer

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Stage IIIa non-small cell lung cancer indicates extension of the primary tumor either to chest wall or proximally and/or mediastinal lymph node involvement. This significantly worsens the prognosis. T3 tumors can be completely excised with a 30-50 % five year survival rate if no nodes are involved. Adjuvant chemotherapy has not been demonstrated to improve survival and adjuvant radiotherapy decreases loco-recurrence rate without affecting survival. Mediastinal lymph node involvement identified preoperatively has a very poor prognosis with less than 10 % of such patients cured following surgical resection. Studies are underway to assess the value of induction chemo/radiotherapy for this stage of disease. Mediastinal disease discovered only at the time of surgery should be resected but the ultimate five year survival rate cannot be expected to be greater than 30 %. Adjuvant radiotherapy is often employed to decrease locoregional recurrence rate.

Surgeons must be very selective in offering surgical resection for patients preoperatively identified to have stage IIIa disease and must be able to ensure that a complete resection is possible.

Arch Bronconeumol 1992; 28:321-323

Locally advanced lung cancer

Locally advanced lung cancer (stage IIIa, IIIb), where the primary tumor is proximal, has invaded adjacent structures or organs or when mediastinal lymph nodes are involved, worsens the prognosis significantly. However, in stage IIIa disease, when surgical treatment results in total removal of the primary tumor and involved lymph nodes, there still is a reasonable chance for ultimate cure.

Stage IIIa disease encompasses T3 tumors (within 2 cm of the carina, invasion of chest wall or mediastinal pleura invasion of pericardium) and N2 disease (ipsilateral mediastinal nodes). This is in contradistinction

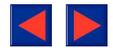
Tratamiento quirúrgico del estadio IIIa del cáncer de pulmón de células no pequeñas

El estadio IIIa del cáncer de pulmón de células no pequeñas indica que el tumor primario se ha extendido a la pared torácica adyacente y/o ha invadido las adenopatías mediastínicas. Este hecho empeora significativamente el pronóstico. Los tumores T3 pueden ser extirpados por completo con una tasa de supervivencia a los cinco años del 30 al 50 % si no existe invasión ganglionar. La quimioterapia adyuvante no ha demostrado aumentar la supervivencia y la radioterapia adyuvante puede disminuir la tasa de recidivas locales del proceso pero no influye en la supervivencia. La invasión mediastínica ganglionar identificada preoperatoriamente encierra muy mal pronóstico de suerte que menos del 10 % de tales pacientes sometidos a resección quirúrgica pueden ser considerados como curados. Hay estudios en curso para establecer el valor de la quimio/radioterapia inducidas en este estadio de la enfermedad. Cuando se descubre la invasión mediastínica al tiempo de verificar la intervención quirúrgica, se debe efectuar la extirpación del tumor, pero no cabe esperar una supervivencia mayor del 30 % al cabo de cinco años. La radioterapia adyuvante es utilizada frecuentemente para disminuir la recidiva local.

El cirujano debe ser muy selectivo al plantear la extirpación quirúrgica de aquellos casos identificados preoperatoriamente de estadio IIIa, debiendo garantizar que la extirpación total del proceso es posible.

to T4 tumors where vital organs are invaded or N3 disease where contralateral mediastinal or supraclavicular nodes are involved.

Total excision can be performed in most T3 tumors and if nodal involvement is absent, a reasonable number of patients (30-50 %) will be cured of their disease. The value of surgery in patients with N2 disease is more controversial. From retrospective analyses, it appears that N2 disease preoperatively identified has a very poor prognosis due to the fact that superior mediastinal disease frequently indicates micrometastatic disease and is less likely to be completely resected. However, N2 disease only identified at the time of surgery signifies less bulky disease with fewer occult



distant metastases which can frequently be completely resected and therefore has the potential to be totally cured by surgical resection alone.

Controversy remains as to be benefits of adjuvant treatment following resection of this more advanced disease. Clinical trials have failed to demonstrate improved survival utilizing either postoperative radiotherapy, postoperative, chemotherapy or a combination of both.

T3 tumors

The curability of T3 tumors varies according to the involved site and whether or not lymph node involvement is present. T3 N0 tumors have a significant cure rate (30-50 %). Once nodal disease is present, the prognosis deteriorates. T3 N2 tumor are rarely cured (less than 10 %).

Chest wall invasion. A T3 tumour by virtue of chest wall invasion still allows a favorable prognosis after resection, specially when there is no associated N1 or N2 disease. If completely excised, T3N0 tumors can yield a 5 year survival in the range of 50 %¹. Once the parietal pleura is involved, complete resection should include the chest wall (vs extra pleural resection) whenever possible. Once nodal involvement is present, the survival rate is much less favorable. Very few T3N2 tumors, even when completely resected, will be cured. Because of this, it is questionable whether this stage of disease, when identified preoperatively, should be considered for resection.

Superior sulcus tumors. It is well known that these tumors, if completely resected, will be cured in about 30 % of cases²⁻⁴. Unfortunately, most patients present with more advanced (T4, N3 or M1) disease, not amenable to curative surgical resection. Although most of these tumors are treated with preoperative radiotherapy followed by surgery, the value of this preoperative treatment has never been proven. Few if any long-term survivors have been documented when N2 disease is present. Additional brachytherapy or postoperative radiotherapy may improve local control^{3,4}.

Proximal airway involvement. Those tumors of the main bronchi within 2 cm of the carina, if completely resected, can certainly be afforded long-term survival.

Utilization of sleeve lobectomy or pneumonectomy for tumors in this location should result in a 50 % 5 year survival if no nodal disease is present^{5,6}.

Diaphragm. Complete resection of T3N0 tumors with diaphragmatic involvement without associated sub-diaphragmatic organ invasion can be carried out with minimal morbidity. However, in most cases the diaphragmatic involvement is diffuse and complete resection cannot be performed.

N2 disease

There has been a surfeit of retrospective reports in the recent literature suggesting that patients iwth N2 disease certainly can be cured if surgical resection is complete. Incomplete resections, with residual gross or microscopic disease rarely lead to 5 year survival⁷⁻¹⁵ (table I).

Selectivity is the important factor in deciding whether or not to offer surgery to patients with preoperatively identifiable N2 disease. Radiologically apparent (CT or chest x-ray) disease, multiple lymph node sites, bulky extra-capsular disease, associated T3 tumors and non-squamous cell histology all appear to adversely affect prognosis.

In the most favorable cases (N2 diseases discovered at surgery), a 30 % 5 year survival rate can be expected when complete surgical excision including mediastinal lymph node dissection has been performed. Unfortunately, few patients with N2 disease will be completely resected (20 % or less).

More bulky N2 disease identified radiologically or at mediastinoscopy is considered by most surgeons to be inoperable. There has been a recent flurry of activity examining the role of induction (neoadjuvant) treatment combined with surgical excision for this more advanced type of N2 disease. Preoperative radiotherapy, and/or chemotherapy have been utilized in an attempt to shrink the tumor prior to surgical excesion¹⁶⁻²¹ (table II). At present, this is an approach that should be reserved for clinical trials although 5 year survivals appear to be enhanced. At Memorial Sloan-Kettering Cancer Center and the University of Toronto induction chemotherapy utilizing mytomycin, vinblastine and cisplatinum have produced a 70 % response rate to this drug treatment. Approximately 50 % of all patients were then comple-

TABLE I
Results of surgical resection of patients with N2 non-small cell carcinoma. Postoperative treatment varied

Author	Cases	5-YT Survival (%)	Identified adverse factors
Gosetti ⁸	79	29.7 Squamous	Multiple N2 sites
Sawamura ¹²	107	38.5 Squamous 22.7 Adeno	T3 N2 Inc. complete resection
Martini ¹⁰	151	30.0 Squamous	"Clinical" N2
Naruke ⁹	218	24.2 Squamous	Inc. resection
Pearson ¹⁴	141	24.0 N2ve med	+ VE mediastinoscopy
LSCG ¹⁵	163	9.0 + ve med 25.0 (3 Yr.)	Multiple N2 sites Multiple sites



TABLE II
Recent results of neoadjuvant therapy followed by surgery for "unresectable" IIIa patients

Author	Neoadjuvant regimen	Patients resected/ total patients	Operative mortality	MST (mos)
Martini ¹⁶	MVP	28/41 (68 %)	3,5 %	19
Egan ¹⁷	CAP + XRT	19/39 (48.7 %)	0	12
Faber ¹⁸	5-FU + PLAT + XRT ± VP-16	62/130 (47.64 %)	5 %	14
Weiden ¹⁹	5-FU PLAT + XRT	46/84 (54 %)	0	10.5
Burkes ²⁰	MVP	22/39 (59 %)	9.2 %	19
Swog ²¹	VP-16-PLAT + XRT	20/40 (50 %)	15 %	NS

MST: Median survival time (months).

tely resected. The 3 year survival rate following such treatment is approximately 35 % and the estimated 5 year survival rate between 15 and 20 %, much better than those seen in patients treated by surgery alone. The ultimate value of this treatment must inevitably be compared with more standard treatment for this stage of disease, radiotherapy or radiotherapy plus chemotherapy, a 5 to 15 % 5 year survival is reported in selected cases. Ultimately, the standard treatment-radiotherapy with or without chemotherapy will have to be compared with this more aggressive surgical treatment program. Radiotherapy alone can effect a 12 month median survival and a 5 to 15 % five year survival in selected cases of this more advanced disease.

Conclusions

Surgery for stage IIIa lung cancer can afford a cure for selected patients. The morbidity of such surgery is necessarily increased by virtue of the advanced stage of the disease, the utilization of induction chemotherapy programs, the extensive nature of the surgery including enbloc resection and pneumonectomy and the fact that most patients presenting with lung cancer are in their sixth or seventh decade.

It is important before embarking on a treatment program for locally advanced lung cancer that the patient be screened for metastatic disease in other sites, especially: adrenal, brain, contralateral lung, bone and liver. Whenever N2 disease is identified preoperatively, this should be confirmed at mediastinoscopy and N3 disease should be ruled out. In such cases of preoperatively identified N2 disease, considerations should be given to an induction chemotherapy (chemo/radiotherapy) program prior to consideration of a surgical approach to the problem.

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