

## Prolonged Survival After Extracranial Metastasectomy From Synchronous Resectable Lung Cancer

Vincenzo Ambrogi, MD, Giuseppe Tonini, MD, and Tommaso Claudio Mineo, MD

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**Background:** Combined resection of solitary synchronous brain metastases and non–small-cell lung cancer has been shown to be successful. Thus, we proposed combining the surgery of solitary, extracranial metastases, and resectable lung cancer.

**Methods:** Between March 1987 and December 1994, surgery was performed on nine patients with non–small-cell lung cancer with synchronous, solitary, extracranial, or distant metastasis: adrenal (n = 5), cutaneous (n = 2), axillary lymph node (n = 1) and kidney (n = 1). Criteria for operating on these patients included: primary tumor that was locally resectable in a radical manner, non–small-cell histology, no preoperative evidence of N2 disease, complete resection of histologically proven metastasis, and absence of other metastases found with computed tomography or bone scan.

**Results:** Resection of the primary tumor and solitary metastases was achieved in all patients. Primary tumor was always resected by lobectomy. No mortality or major morbidity was reported. Five-year survival rate was 55.6%. Five patients who had adrenal (n = 3), or skin (n = 1), or axillary (n = 1) metastases, survived more than 5 years. All N2 patients (n = 2) died.

**Conclusions:** The presence of solitary, distant metastasis should not be considered, per se, a factor for denying surgery for locally resectable, non–small-cell lung cancer. Unexpected, prolonged survival was demonstrated in our limited series.

**Key Words:** Lung cancer—Adrenal metastasis—Skin metastasis—Surgery.

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Distant metastases from non–small-cell lung cancer (NSCLC) are generally multiple, disseminated, and associated with a poor outcome.<sup>1</sup> Treatment with chemotherapy has improved survival only marginally.<sup>2,3</sup> Metastases often can be the primary manifestation of an occult cancer<sup>1–4</sup> and may develop as a solitary site of distant metastasis from lung cancer in a certain percentage of patients.<sup>5,6</sup> As proposed in the cases of brain solitary metastasis,<sup>4–6</sup> surgery for solitary metastatic lesion in patients with controlled or controllable regional disease could be reasonably hypothesized.

The finding of long-term survival in our patients who underwent simultaneous resection of metastasis and non–small-cell lung cancer stimulated our interest in the

role of surgery in this particular situation. We analyzed our experience by focusing attention on the effects of surgical excision on long-term survival.

### MATERIAL AND METHODS

Among the 358 patients who had radical operations for NSCLC between March 1987 and December 1994, we retrospectively identified nine patients who were operated on with synchronous resection of solitary extracranial distant metastasis; these included adrenal (n = 5), skin (n = 2), ipsilateral axillary lymph node (n = 1), and kidney (n = 1). Table 1 summarizes patient characteristics and clinical data. The median age was 58.7 years (range 45–69 years). Despite the presence of a single proven metastasis, all these patients were considered for surgery for at least one of the following reasons: primary tumor was considered resectable without residual local disease, non–small-cell histology, no preoperative evidence of N2 disease, absence of other metastases by computed tomography (CT) or bone scan or clinical

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From the Department of Thoracic Surgery, Tor Vergata University, Rome, Italy.

Address for correspondence and reprints: Prof. Tommaso Claudio Mineo, Cattedra di Chirurgia Toracica, Ospedale S. Eugenio, p.le Umanesimo 10, 00144 Rome, Italy; Fax: 39-06-592-2681; E-mail: mineo@med.uniroma2.it.

**TABLE 1.** Characteristics of patients with lung cancer and extracranial metastases

No.	Sex	Age	History	Location of lung cancer	pTN	Primary treatment	Location of metastasis	Diameter (cm)	Status	Follow-up (mos)	Site of first recurrence
1	F	48	Adc	LUL	T3 N0	S Cht	Scalp skin	4	Alive	74	None
2	M	69	Sq	LUL	T3 N0	S Cht	Thigh skin	6	Dead	8	Lung
3	M	63	Adc	LUL	T2 N0	S Cht	Ipsilateral Adrenal	7	Alive	66	None
4	M	57	Lc	RUL	T2 N0	S	Ipsilateral Adrenal	5	Alive	116	None
5	M	61	Lc	RLL	T2 N0	S Cht	Ipsilateral Adrenal	5	Alive	90	None
6	M	64	Sq	LUL	T3 N1	S Cht	Contralateral Adrenal	8	Dead	30	Brain
7	M	57	Sq	RLL	T3 N2	S Cht	Contralateral Adrenal	10	Dead	18	Brain
8	M	45	Sq	LUL	T3 N1	S Cht	Ipsilateral Axillary Lymph node	2	Alive	96	None
9	M	64	Lc	RLL	T2 N2	S Cht Rxt	Ipsilateral Kidney	6	Dead	36	Systemic

Adc, adenocarcinoma; Sq, squamous cell carcinoma; Lc, large cell carcinoma; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RLL, right lower lobe; S, surgery; Cht, chemotherapy; Rxt, radiotherapy.

examination, good general conditions (Karnofsky index > 90). To assess the operability, all patients underwent preoperative total body CT scan, fiberoptic bronchoscopy, and bone scan. Cervical mediastinoscopy was performed whenever CT showed enlarged mediastinal lymph nodes.

Synchronous metastases were documented either prior to primary tumor discovery (n = 2) or during preoperative assessment (n = 7). The metastatic nature of each was confirmed by histological demonstration. Complete resection of skin and lymph node lesions was considered satisfactory. Adrenal lesions were biopsied through a CT-guided needle during the preoperative study. In one patient, a 6-cm right kidney lesion was discovered during the preoperative study; the radiological appearance suggested a malignant neoplasm and the CT-guided biopsy was positive for large cell histology that was compatible with the primary tumor.

Lung cancer patients whose cancer had direct involvement of the chest wall and the skin were excluded from the study. No metastases on the site of surgical incisions were recorded. Evidence of other potentially metastasizing malignancies was excluded for all the patients belonging to the study group. In all patients, primary surgery implied radical cancer resection and systematic dissection of mediastinal lymph nodes (Table 1).

## RESULTS

Resection of the primary tumor and solitary metastases was achieved in all patients. Type of lung resection

was left upper lobectomy (n = 5), right lower lobectomy (n = 3), and right upper lobectomy (n = 1). Histology was large cell carcinoma (n = 3), adenocarcinoma (n = 2), and squamous cell carcinoma (n = 4). At systematic dissection, mediastinal lymph nodes were positive in two instances (Table 1). Each of these two patients presented only one positive lymph nodal station: subcarinal for case number 7, and right tracheobronchial angle for case number 9 not evidenced with CT. Except for lymph nodal lesions, metastasectomy was always performed in a second session in the same hospital stay after a mean period of 10.5 days. Adrenal metastases were always resected through a laparotomic approach and required an average of 5.5 days for complete recovery.

Mean maximal diameter of adrenal metastasis was 7.0 cm (range 5–10 cm). Skin metastases resection was simple in all patients and did not require rotation flap or major plastic surgery. The ipsilateral axillary lymph node was resected before lung surgery. Nephrectomy was accomplished 14 days after the lung procedure and the patient was discharged 7 days later. No mortality or major morbidity was reported in any of the patients. Adjuvant chemotherapy was performed in all patients for 6 months after surgery; only one patient refused the treatment. Radiotherapy was performed in only one case at the site of nephrectomy because of unclear resection margins.

Mean 5-year survival rate was 55.6%. Five patients are alive and free of disease at more than 5 years from the operation: adrenal (n = 3), skin (n = 1), and axillary (n = 1). All four patients who developed

reprise of disease died shortly after the diagnosis. The pattern of the first recurrence after metastasectomy is described in Table 1. Both patients with N2 disease died after 18 and 36 months, respectively.

## DISCUSSION

Distant metastatic (M1) disease is generally considered a contraindication for resection of the primary tumor because of poor outcome.<sup>1</sup> Most patients who have been diagnosed with M1 disease have multiple sites of metastases identified, and their survival is measured in months despite chemotherapy.<sup>2,3,7-11</sup> Nevertheless, there is a definite subset of patients with primary resectable tumor and with a sole site of metastatic disease that may benefit from synchronous resection of both lesions. It has already been demonstrated that patients with solitary brain metastasis who undergo resection of the primary tumor and brain metastasectomy can reach 5-year survival rates of between 15–30%.<sup>4,12</sup> Furthermore, complete resection of the primary lung cancer is the major determinant of survival in patients who undergo resection of brain metastases.<sup>4</sup>

The possibility of having a sole site of extracranial metastases in patients with operable lung cancer and proven single metastasis is generally considered quite low. Ettinghausen and Burt<sup>13</sup> deemed the rate of solitary adrenal metastases to be around 1.62% and La Porte et al. at 3.5%.<sup>14</sup> On the other hand, Luketich et al.<sup>15</sup> observed that 7% of the patients with metastatic disease from NSCLC have a solitary metastasis after full evaluation. Furthermore, Quint et al.<sup>16</sup> have recently discovered that in a total of 72 patients with M1 disease with newly diagnosed lung cancer, more than 50% of the patients (n = 48) had metastasis restricted to one body part.

According to this last report, surgery for extracranial solitary metastases may have a rationale. The finding of long-term survival in our study of patients who underwent simultaneous resection of metastasis and NSCLC stimulated our interest in the role of surgery for this situation. The long-term survival of our highly selected cohort of patients is quite encouraging. We observed five out of nine patients who are still alive and free of disease after a follow-up longer than 5 years.

The adrenal gland is a frequent site of metastases from NSCLC. CT scans of the abdomen performed during the staging of NSCLC revealed adrenal metastases in 5% to 10% of patients.<sup>17-19</sup> There are several reports in the literature of long-term survivors after adrenalectomy for isolated metastasis.<sup>20-22</sup> Ayabe et al.<sup>20</sup> suggested that adrenalectomy may provide good results when all of the following conditions are present: controlled or control-

lable primary tumor, no evidence of other distant metastatic lesion, unilateral and completely resectable adrenal metastasis, and good physical condition of the patient.

Reports of simultaneous removal of metastatic distant lymph nodes are uncommon. Luketich et al.<sup>15</sup> described resection of metachronous metastatic lymph nodes from different sites in six patients: supraclavicular (n = 2), cervical (n = 2), groin (n = 1), and axillary (n = 1). In the present series, patients with supraclavicular lymph nodes were not considered because they did not belong to the M1 disease category. There were, however, two patients with positive ipsilateral supraclavicular nodes who survived more than 1 year after presumed radical surgery. The only patient we operated on who had positive ipsilateral axillary nodes is still alive and free of tumor after 96 months from the procedure (Table 1).

The presence of skin metastases is another condition that is considered a sign of an inoperable disease. Nevertheless, for cases with ascertained solitary deposits, there seems to be a rationale for surgery: indeed it might be limited to only one site and amenable to surgical treatment.

Observations have shown that a few patients have survived for many years<sup>23,24</sup> in spite of the bad prognosis related to the presence of skin metastases. In our opinion, the conditions for longer survival are related not only to the primary tumor (tumor node stage and total eradication), but also to the characteristics of metastasis: solitary, resectable lesions in the absence of other extracranial deposits. As for adrenal metastasis, skin metastasectomy may also be performed to provide pain-relief.

This study sample was obviously small and therefore no significant statistical evaluation is possible. The tumor node status strongly influenced prognosis: both patients with N2 disease died with a median survival of 27 months. This finding suggests the necessity of routine mediastinoscopy to assess N2 disease in patients with M1 disease even in the absence of positive imaging. The presence of N2 disease in these patients should result in a decision to avoid surgical resection.

In conclusion, the presence of a solitary, distant metastasis should not be considered in itself as a factor for denying surgery for locally, resectable NSCLC. Our experience of prolonged survival confirms that metastasectomy and radical resection should be performed for the primary tumor in the absence of N2 involvement.

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