Follow-up in Lung Cancer* 
How Often and for What Purpose?

Riad N. Younes, MD, PhD; Jefferson L. Gross, MD; and Daniel Deheinzelin, MD, PhD

Objectives: The present study evaluates the cost-effectiveness of two follow-up routines: a strict follow-up with frequent visits, imaging, and laboratory examinations was compared to a follow-up with infrequent visits that were scheduled mainly on the basis of the patient’s symptoms.

Methods: A retrospective evaluation was undertaken of 130 patients who underwent a complete resection of non-small cell lung cancer (NSCLC). All patients had complete follow-up for at least 2 years after their operation. The patients were separated into two groups: strict (n = 67), with a routine follow-up policy; and symptom (n = 63), seen on a symptom-oriented basis. The costs of the follow-up routines and the yield of each schedule were compared between the two groups.

Results: There were no significant differences in the disease-free interval until the first detection of recurrence. In most patients, metastatic diseases were diagnosed on the basis of symptoms, rather than by routine tests. The patients who had recurrent cancer diagnosed after surgery had a dismal survival rate irrespective of the follow-up schedule. The majority of patients with recurrence died of malignancy within a 2-year period. The costs of strict vs symptom follow-up were significantly different, because of the greater number of routine imaging procedures performed in patients having strict follow-up. On the other hand, when we analyzed only the frequency of hospitalization and the cost per day of hospital treatment for medical problems other than cancer recurrence, the patients in the strict group had a less expensive follow-up than the patients in the symptom group.

Conclusions: The present study showed that a more cost-effective routine follow-up scheme should be advised for patients with completely resected NSCLC, without affecting overall outcome. Routine imaging follow-up is of questionable value, and it may be indicated only in academic settings.

Key words: costs; follow-up; lung cancer; surgery

Abbreviations: NSCLC = non-small cell lung cancer

Lung cancer is an extremely aggressive neoplasia, with the majority of admitted patients presenting with metastatic dissemination. When the disease is diagnosed early, the best available treatment is a complete resection of local disease. However, only 40 to 50% of patients currently

survive for > 5 years after the operation,¹⁻³ and most die of systemic metastases. Local recurrence may occur in 5 to 20% of patients, depending on the pathologic staging of the tumor.⁴ Second primary tumors are often observed in patients successfully treated for lung cancer (2 to 15%),³,⁵ and they are potentially curable with further treatment in 40% of cases.⁶,⁷

Fifty percent of all recurrences are diagnosed in the first 24 months after curative treatment, and approximately 90% of all recurrences are diagnosed...
within 5 years. Despite such high figures, a follow-up routine is not yet established, with a wide range of visits, frequencies, tests, and examinations being ordered at each individual institution. The rationale for each test and the cost-benefit of intensive routine follow-up, as compared with evaluation oriented solely by the patient's symptoms, are still unclear. A more defined policy has to be introduced in order to tailor the follow-up schedule to the patient's situation, therefore maximizing the benefit against a reasonable cost.

Follow-up routines after complete treatment for cure have been evaluated for other tumors, such as breast carcinoma and colorectal cancer, but few comparative evaluations for lung cancer patients have been published. The objective of the present study was to review the influence of strict follow-up after lung cancer resection (as opposed to symptom-oriented follow-up) on the outcome of patients with non-small cell lung cancer (NSCLC). The recurrence rate, site of recurrence, and time distribution of recurrences were evaluated. The capacity of routine tests to detect recurrences, the results of the early detection of tumor spread, and salvage therapy were also assessed. The overall cost-benefit was determined, and a routine follow-up policy will be established on the basis of the findings of this study. This study protocol limited the analysis to the first 2 years after the resection of the primary tumor, to assess the effectiveness of follow-up during the period when most centers recommend more frequent visits and tests to the patients. Usually the interval between visits and tests is increased to two to three visits per year until the fifth year of follow-up. After that period, follow-up is scheduled on a yearly basis in most centers.

**Materials and Methods**

A retrospective evaluation was undertaken of patients who underwent both operative and pathologic complete resection of NSCLC at the Department of Thoracic Surgery from June 1983 until June 1993. Inclusion criteria were a complete follow-up for at least 2 years after operation or until death (if it occurred within this period), with a detailed record from the patient's chart of each procedure performed during this period. All charts were reviewed for the following: age; gender; preoperative cardiovascular, lung, renal, hepatic, or other diseases; type of resection; surgical-pathologic stage; histology; adjuvant therapy; type of recurrence, site, and disease-free interval; treatment of recurrence; salvage and control rates; occurrence of nonneoplastic health problems and mode of detection and treatment; overall survival and disease-free survival; and cause of death. The costs of follow-up were calculated for each case on the basis of the cost of each described procedure. To make all values comparable, all individual costs were updated to their more recent costs at our institution, regardless of the year when the patient was admitted and operated on. At our institution, the estimated average cost in US funds for each procedure is as follows: consultation, $20; chest radiograph, $50; CT scan of the chest and upper abdomen, $200; liver function test, $30; and average inpatient medical treatment for health problems (not including chemotherapy or radiation therapy), $300/d.

The patients were separated into two groups: group 1 (strict, n = 67), with routine follow-up policy shown in Table 1; and group 2 (symptom, n = 63), seen at our hospital on a symptom-oriented basis, with ≤ 3 consultations per year scheduled by the attending physician in the first 2 years after resection. The patients were submitted to the different patterns of follow-up routine established at our department. The routine was changed for all physicians after 1990, when a strict follow-up was established as a standard approach for all patients with lung cancer. The patients were studied after they were discharged from the hospital following their operation. The patients having a recurrent disease diagnosis were staged, if they had local recurrence amenable to surgery, they underwent resection. However, when the patients had unresectable disease or disease that was clinically inoperable, local recurrences were treated with radiation therapy. Patients who were clinically fit and had metastatic disease received chemotherapy, unless they had CNS metastases. This group of patients received only radiation therapy to the brain and supportive care.

**Statistical Analysis**

The means in the two groups were compared by Student's t test. Categorical parameters were compared by Fisher's Exact Test. Disease-free survival curves were established by the Kaplan-Meier method and compared between groups using Breslow and log-rank analyses. All differences were considered significant at p < 0.05.

**Results**

This retrospective study included 130 consecutive patients who underwent a complete resection of NSCLC (lobectomy or pneumonectomy with systematic mediastinal lymph node dissection) with a complete follow-up for 2 years or until death, if it occurred within 2 years of the operation. All patients in our hospital routinely have an extensive preoper-
ative staging of lung cancer that includes a chest and upper abdomen CT scan, a bone scan, and a brain CT scan to detect asymptomatic distant metastases. Despite these thorough preoperative imaging procedures, we still have an overall 20% 2-year distant recurrence rate in our patients undergoing a curative operation. Table 2 shows the patient characteristics of the two groups. There were no significant differences between the groups. Table 3 shows the number of consultations and ancillary examinations performed in each group during the first 24 months, which was significantly higher in the strict group (p < 0.001 for all comparisons).

Table 4 shows the follow-up data from the two groups. The number of outpatient consultations was greater in the strict group than in the symptom group, as were the number of radiologic evaluations and laboratory tests for liver function. Metastatic disease was detected in the following sites: strict group, CNS (n = 3), liver (n = 2), bone (n = 3), lung (n = 3), and multiple sites (n = 2); symptom group, CNS (n = 4), liver (n = 2), bone (n = 5), lung (n = 2), adrenal (n = 1), and multiple sites (n = 2). The median survival after recurrence was 7.9 months for the strict group and 6.6 months for the symptom group (p = 0.219).

Figure 1 shows disease-free survival curves for the two groups during the 24-month period. There was no significant difference between the two groups. Table 5 depicts the overall results of diagnosis and treatment.
management of health problems in the two groups. When compared to the strict group, a significantly greater number of patients in the symptom group had health problems diagnosed in the emergency room setting and were treated in-hospital.

The salvage rate for recurrent lung cancer was similar in both groups, with only one patient in the strict group alive and free of disease 7.6 months after diagnosis of systemic recurrence, and one patient alive with disease for 5 months after treatment for local recurrence. All other patients in the strict group were dead of disease after recurrence. In the symptom group, only two patients were alive with disease during the study period. All other patients were dead of recurrent cancer. There was no significant impact of an earlier diagnosis on the survival rate in either group (p = 0.135).

On the other hand, the strict follow-up schedule helped detect earlier health problems other than cancer recurrence, which significantly decreased the number of emergency room admissions for clinical diseases, and consequently prevented the late diagnosis of health problems, as well as the number of in-hospital days for the treatment of these problems. The difference between the two groups was highly significant. The total costs of the patients included in each group are shown in Table 6.

### Table 5—Management and Outcome of Health Problems Detected During Follow-Up

<table>
<thead>
<tr>
<th>Categories</th>
<th>Strict</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health problems detected at emergency room, %</td>
<td>45</td>
<td>79</td>
</tr>
<tr>
<td>Episodes detected at emergency room*†</td>
<td>0.6 ± 1.5</td>
<td>1.9 ± 1.6</td>
</tr>
<tr>
<td>Health problems treated as outpatient, %†</td>
<td>88</td>
<td>65.6</td>
</tr>
<tr>
<td>Health problems treated as inpatient, %†</td>
<td>12</td>
<td>34.4</td>
</tr>
<tr>
<td>Days inpatient for health problems*†</td>
<td>0.68 ± 1.44</td>
<td>1.92 ± 3.47</td>
</tr>
<tr>
<td>Deaths from causes other than cancer, No.</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Second primary tumors detected, No.</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*pPresented as mean ± SD.

†p < 0.001.

### Table 6—Total Costs of Patients During the 24-Month Follow-up Period*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Categories</th>
<th>Strict</th>
<th>Symptom</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient</td>
<td>1406.86 ± 241.2</td>
<td>402.85 ± 160.58</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Radiology</td>
<td>1107.46 ± 232.12</td>
<td>238.88 ± 133.96</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>205.97 ± 434.45</td>
<td>576.19 ± 1043.83</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2720.30 ± 665.92</td>
<td>1217.94 ± 1113.16</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

*Values are given in US $; mean ± SD.

The early detection of recurrent cancer would be a very important approach, if one could influence the outcome of patients having a recurrent cancer diagnosis. Our study, as well as studies by others, demonstrate the dismal prognosis for patients with recurrent lung cancer, regardless of the therapy instituted after the detection of metastases. The vast majority of patients (91.4%) with recurrences were dead of their malignant disease within the 2-year period of our study; there was no significant difference in the control rate for either group after cancer recurrence. The early detection of recurrent disease, at least in lung cancer, does not translate into better control or longer survival for the patients. The present study could not detect a potential benefit from the early detection of recurrent disease by frequent tests and visits. Quality of life, on the other hand, was not assessed by our protocol, although conceivably one could suppose that an earlier initiation of chemotherapy might sustain quality of life for a longer period. These results are in accordance with recently published retrospective data. However, in that study, the follow-up policies were not predetermined, as they were in our study. Notwithstanding such differences, until we have a more efficient systemic therapy for NSCLC, recurrent malignancy will be treated on a palliative basis, with no significant impact on overall survival.

A follow-up routine of patients who undergo complete resection of NSCLC is not universally agreed on, and there are wide variations in routine procedures among different services and institutions. Our strict routine follow-up scheme was significantly more efficient in helping the attending physician...
detect (in a timely fashion) medical health problems other than cancer recurrences. These health problems are very common in patients with advanced age (characteristic of the lung cancer population), as well as in heavy smokers undergoing surgical treatment of their malignant disease. The identification of benign health dysfunction efficiently decreased the hospitalization rate and emergency room admissions in the strict group, as compared to the symptom group. Deaths from causes other than cancer were more frequent in the symptom group. One could speculate that an earlier identification and treatment of mild health problems could prevent the patient and his or her family from overlooking significant and potentially disabling (or fatal) medical problems, thereby increasing the likelihood of therapeutic control and reversal of the disease process in an outpatient setting. Health counseling and medical watch is a conceivable benefit of frequent medical consultation in this patient population. In such scenarios, the specialized surgeon or pulmonologist from the cancer attending team appears to be more capable of differentiating such health problems from problems derived from the cancer itself or from the surgical therapy used.

The overall costs of strict follow-up were significantly greater than those of symptom follow-up, mainly because of the greater number of routine imaging procedures performed and the additional consultations and liver function tests for the strict group. On the other hand, when looking only at the frequency of hospitalization and the cost per day of hospital treatment for medical problems other than cancer recurrence, the patients who were frequently seen (the strict group) had a less expensive follow-up than the patients who waited for symptoms before being seen. The difference in the average number of days in the hospital between the strict group (0.68) and the symptom group (1.92) would represent a projected estimated savings (for the strict group) of $370 per patient. The results of the present study show that a more cost-effective routine follow-up scheme could be advised for patients with completely resected NSCLC, without affecting the overall outcome. Routine imaging follow-up is of questionable value, and it may be indicated only in protocol or academic settings. The new suggested follow-up routine is shown in Table 7. Compared with our previous strict follow-up regimen, this new routine would be as efficient in detecting health problems other than cancer recurrence, with no disadvantages on cancer follow-up and survival rates. The total costs of follow-up would be reduced to 32.2% of the routine strict follow-up. When taking into account the estimated number of potential candidates for complete resection each year (currently > 30,000 patients per year in the United States),16 this new routine would represent a significant decrease in total costs of the follow-up of lung cancer patients.

On the basis of the above considerations, we are in disagreement with a recently proposed follow-up policy by Walsh and colleagues,15 suggested that contact made by a nonspecialized physician or even a nurse practitioner every 6 months should be sufficient. Our data showed that a more frequent visit schedule with a specialized physician consultation can be more cost-effective. However, we agree that nothing more than a chest radiograph is necessary.

The detection of second primary tumors in patients with NSCLC is widely described in the literature. It is estimated to occur in 2 to 15% of patients with lung cancer diagnoses.3,6 Patients who undergo complete resection of their lung tumor usually live longer and, therefore, have a greater likelihood of experiencing a second primary tumor. Routine and strict follow-up could help the physician to scan and detect second primary tumors at an early and, therefore, potentially curable stage. We diagnosed a second primary tumor (laryngeal carcinoma) in only one patient during this short follow-up period (24 months). Longer intervals are usually described for the appearance and diagnosis of second tumors, usually in the range of 5 to 8 years after the treatment of the first primary neoplasia.3,6 A strict follow-up in our patients was not able to detect other tumors in the first 24 months after resection of lung cancer.

To be able to define the most cost-effective method of follow-up for the patient with completely resected lung cancer, the results of this study need to be further validated in a prospective, randomized fashion. Stratification according to the severity of medical problems or according to pathologic stage

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**Table 7—Suggested Routine Tests in Patients for Follow-Up After Discharge From Hospitalization for Complete Resection of NSCLC***

<table>
<thead>
<tr>
<th>Postdischarge Time</th>
<th>Physical Examination</th>
<th>Chest Radiograph</th>
<th>CT Scan</th>
<th>Liver Function Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 wk</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 wk</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 mo</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 mo</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 mo</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 mo</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 mo</td>
<td>X</td>
<td></td>
<td></td>
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</tbody>
</table>

*Former total cost of routine follow-up was $1,430 for 24 mo; new total cost of routine follow-up is $460 for 24 mo (67.8% less expensive).
should be included in those studies to define the subgroups of patients that could benefit from intensive or less intensive follow-up schedules.

REFERENCES